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RHEUMATIC HEART DISEASE IN SOUTH INDIA

AN ELECTROCARDIOGRAPHIC STUDY

P. KUTUMBIAH, B.A., M.D., M.R.C.P. (LOND.)

AND

T. K. RAMAN, M.D., D.T.M. (CAL.)

Department of Medicine, Andhra Medical College and King George Hospital, Vizagapatam.

The recognition of the existence of rheumatic heart disease in India is of recent date. We have many critical studies of the clinical aspects of rheumatic heart disease as it occurs in different parts of this country. A search of the literature does not reveal a single comprehensive electrocardiographic study of the disease. Hughes and Yusuf (1930) in their study of heart disease in the Punjab with special reference to mitral stenosis published a number of electrocardiograms illustrative of the various cardiac abnormalities noted by them. Raman (1937 and 1940) published electrocardiographic studies of auricular fibrillation, extra-systoles and auricular flutter including those of rheumatic ætiology, based on the records obtained in the King George Hospital, Vizagapatam. Hitherto, electrocardiographic studies in this country were handicapped by the lack of normal standards for Indian subjects. Vakil (1940 and 1941) has supplied this long felt want by the publication of his analysis of 300 normal electrocardiograms of Indian subjects. Lewis (1931) has stressed the fact that the electrocardiogram has very little to do with valvular lesions as it is primarily concerned in the investigation of the cardiac muscle and that valvular lesions influence the form of the electrical curves only in so far as they affect the muscle. Certain changes in the size of the individual chambers of the heart are regularly associated with cardiac valvular lesions. Electrocardiogram demonstrates the particular effect of each valvular lesion on the heart in a graphic manner, and certain electrocardiographic changes appear with such regularity that it can be used as an aid in the differential diagnosis of valvular lesions (Berliner and Master, 1938). The present study is mainly intended to analyse the electrocardiographic changes characteristic of the valvular lesions met with in rheumatic heart disease in South India and to ascertain their diagnostic value.

Method of Study

The study was limited to cases which showed the well-acknowledged clinical signs of rheumatic infection. In most cases the diagnosis was supplemented by x-ray examination. Electrocardiograms of 173 cases of heart disease of rheumatic ætiology which were under observation in the wards in the King George Hospital, Vizagapatam, between 1931-1940 were collected and 263 electrocardiograms were analysed. Only correctly standardised electrocardiograms were included in this series. For the purposes of this study the cases were classified on an anatomical and a functional basis as follows:—

Group I. Cases showing no evidence of any cardiac lesion or of simple mitral insufficiency (8 cases).

Group II. (*a*) Cases of mitral stenosis with no failure of compensation (17 cases).

(*b*) Cases of mitral stenosis with evidence of failure of compensation (15 cases).

Group III. (*a*) Cases of mitral stenosis and mitral insufficiency with no failure of compensation (15 cases).

(*b*) Cases of mitral stenosis and mitral insufficiency with failure of compensation, including one case of mitral and tricuspid stenosis with failure of compensation (68 cases).

Group IV. Cases of mitral stenosis and mitral insufficiency with aortic insufficiency and failure of compensation (11 cases).

The electrocardiograms were carefully analysed as to the changes in the P wave (auricular complex), the duration of the P-R interval (conduction time), the initial ventricular deflection (Q wave), the main ventricular deflection (QRS), the final ventricular deflection (T wave), the rate, rhythm and the abnormal contractions arising from ectopic foci. The results of this analysis are presented in the various tables (*vide infra*).

The electrocardiograms were all taken on the Cambridge English Model Electrocardiograph with the patient in the semi-recumbent posture. The criteria for the interpretation of electrocardiograms recommended by the Committee of the New York Heart Association (1942) and the standards obtained by Vakil (1940 and 41) for Indian subjects have been followed in this article except where otherwise stated.

Incidence

Age and Sex—The incidence of age and sex is shown in Table I.

TABLE I—SHOWING DISTRIBUTION ACCORDING TO AGE AND SEX

Age	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	Above 40	Total
Males ..	0	14	21	40	30	13	13	3	4	138
Females ..	0	9	2	10	5	6	1	2	0	35
	0	23	23	50	35	19	14	5	4	173

The minimum age was 6 and the maximum 45, the greatest incidence was between 15 and 25; 46 cases were in children (below 15 years) and the ratio of males to females was 3·8:1.

Nationality and Religion—Table II shows the distribution according to nationality and religion.

TABLE II—SHOWING DISTRIBUTION ACCORDING TO NATIONALITY AND RELIGION.

Indians	*Males*	*Females*	*Total*
1. Hindus ..	130	35	165
2. Mohemedans ..	7	0	7
3. Christians ..	1	0	1
	138	35	173

P WAVE (AURICULAR COMPLEX)

According to Pardee (1941) the three features frequently observed in a P wave associated with mitral stenosis are: (1) The height of the P wave is excessive in 75 per cent of cases of mitral stenosis with normal rhythm and is sometimes found as large as 5 mm. (2) The duration of the P wave is excessive being over 0·10 second in 85 per cent of the records. (3) Notching of the P wave occurs with unusual frequency, being found in about 80 per cent of records from hearts with mitral stenosis and in only about 30 per cent of records from normal individuals.

TABLE III—ANALYSIS OF THE P WAVE SHOWING AMPLITUDE, DURATION AND NOTCHING.

Class	*Number of cases*	*Average amplitude in m.m.* L I.	L II.	L III.	*Duration in seconds.* L I.	L II.	L III.	*No. of cases with notching* L I.	L II.	L III.	*Notched waves.*
I	7	2·14	3·14	1·42	0·06	0·06	0·06	0	0	0	0
II (*a*)	51	2·47	4·07	2·09	0·06	0·08	0·06	2	1	2	10%
(*b*)	17	2·41	4·29	2·35	0·06	0·09	0·04	2	3	0	30%
III (*a*)	15	3·26	5·13	2·80	0·07	0·09	0·06	5	1	0	40%
(*b*)	57	3·35	4·86	2·05	0·07	0·08	0·05	7	7	1	26·8%
IV	11	2·81	3·81	2·18	0·05	0·06	0·04	2	0	0	18·1%
	158	2·74	4·04	2·14	0·06	0·07	0·05	18	12	3	

Amplitude—Table III gives the data regarding the amplitude, duration and incidence of notching in the P wave in the three standard leads for the various groups. Vakil (1941) found the average amplitude of the P wave for Indian subjects of all decades in the three standard leads (L I, L II, L III) to be 0·89 mm., 1·35 mm., and 0·76 mm., respectively and the range of the amplitude, 0·2 to 3·1 mm. According to Lewis (*loc. cit.*) the average values of P for the standard leads are 0·52 mm., 1·16 mm. and 0·81 mm. respectively and the range of the amplitude 'a trace' to 1·7 mm. Thus it will be seen that both the average and the maximum amplitude of the P wave for normal Indians appear to be definitely higher than that of the normal in western countries. This was kept in mind in assessing the amplitude of the P wave in this study. The average amplitudes of the P wave for the groups associated with mitral stenosis in the three leads were 2·86, 4·43 and 2·29 mm. respectively. Lewis (*loc. cit.*) has indicated 4 mm. as the maximum amplitude of the P wave in mitral stenosis. Pardee (1941) stated that this wave was sometimes found as large as 5 mm. The marked increase in the amplitude of the P wave met with in mitral stenosis simple or associated with lesions of other valves is better appreciated by a study of the percentage frequencies of the amplitude of the P wave as shown in Table IV.

TABLE IV—SHOWING AMPLITUDE OF THE P WAVE (PERCENTAGE FREQUENCIES) IN LEAD II.

Amplitude range (in mm.)	*Average value (normals)* (VAKIL)	*Group I*	*Group II (a)*	*Group II (b)*	*Group III (a)*	*Group III (b)*	*Group IV*
−1 to 0	1·0	Nil	Nil	Nil	Nil	Nil	Nil
0 to 1	40·5	Nil	Nil	Nil	Nil	Nil	Nil
1 to 2	43·5	28·50	9·80	5·88	13·34	5·25	18·18
2 to 3	13·0	42·85	41·10	35·29	6·66	28·07	9·09
3 to 4	2·0	14·29	19·60	17·65	20·00	15·78	45·46
4 to 5	Nil	14·29	9·80	23·54	20·00	21·10	27·27
5 to 6	Nil	Nil	7·84	Nil	6·66	7·01	Nil
6 to 7	Nil	Nil	3·92	17·64	20·00	10·52	Nil
7 to 8	Nil	Nil	7·84	Nil	13·34	10·52	Nil
8 to 9	Nil	Nil	Nil	Nil	Nil	Nil	Nil
9 to 10	Nil	Nil	Nil	Nil	Nil	1·75	Nil

In the groups associated with mitral stenosis, the percentage of P waves over 3 mm. range from 50 to 80, but only 2 per cent of the P waves in normals are over 3 mm. in amplitude. In 36 (23·84 per cent) out of the 151 cases with mitral stenosis and other associated valvular lesions, the P wave was found to be over 5 mm. Berliner and Master (*loc. cit.*) in their study of mitral stenosis found that marked increase in the amplitude of the P wave was not frequent in cases of uncomplicated mitral stenosis. But when it did occur, they obtained an anatomical explanation for it by comparison of the postmortem observations with the electrocardiogram. Such a comparison revealed an interesting relationship between hypertrophy of the auricles and the height of the P wave. In half the cases of uncomplicated disease of the mitral valve, there was hypertrophy of the right auricle, besides hypertrophy of the left auricle, and in all these cases there was a high P wave. They inferred that a marked increase in the height of the P wave with notching was pathognomonic of enlargement of both the right and the left auricles. Our study suggests the same conclusion. The percentage of P waves of 5 mm. for the group of mitral stenosis is 18·7, whereas it rises sharply to 40 in the group of mitral stenosis and insufficiency (Group I b). This marked increase in the percentage must be due to some additional factors operating in this group. One of these factors appears to be the enlargement of the right auricle in addition to the left auricle. Enlargement of the right auricle has been noted to occur in many cases of uncomplicated mitral stenosis. When mitral insufficiency complicates mitral stenosis this enlargement of the right auricle becomes a more common feature. Thus in 14 cases of mitral stenosis and insufficiency in which postmortem study were possible (only 3 cases belong to this series) dilatation and hypertrophy of the right auricle were noted in 4 cases and marked dilatation in 7 cases. Another factor which may be operative at least in some of the cases of this group is an associated disease of the tricuspid valve. The studies of Berliner and Master (*loc. cit.*) have shown that mitral stenosis very often occurs in association with lesions of other valves particularly of the tricuspid. Coombs (1924) found mitral stenosis in association with tricuspid valvular disease in 35 (36 per cent) of 97 cases of rheumatic heart disease, Bland *et al* (1935) quoted by Cooke and White (1941) in 30 of 100 cases, Berliner and Master (*loc. cit.*) in 40 (35·4 per cent) of 113 cases and Cooke and White (1941) in 47 (22 per cent) of 217 cases. In a series of 14 cases (E.C.G. was taken only in 3 of these cases) where autopsy was possible we found tricuspid lesion in 4 (28·57 per cent) cases. The average figure is about 30·47 per cent. Assuming an increase in the amplitude of the P wave over 5 mm. as a probable evidence of the enlargement of the right auricle in addition to that of the left auricle as a result of tricuspid insufficiency or stenosis or both, one would expect the percentage of the occurrence of P waves over 5 mm. roughly to correspond to the percentage of the occurrence of mitral in association with tricuspid valve disease. The occurrence of P waves over 5 mm. in this series was 23·84 per cent which is a fairly close approximation to the percentage quoted above of mitral disease, associated with tricuspid disease, based on postmortem data. An absolutely constant relation between the amplitude of the P wave and the degree of auricular enlargement can never be expected as the voltage of the P wave does not depend solely on the size of the auricles but it depends also on the position of the auricles, their relation to the surrounding organs and upon variations in the condition of the auricular myocardium. Unlike mitral insufficiency, aortic insufficiency complicating mitral stenosis seems to have no appreciable effect on the amplitude of the P wave. In the group of 11 cases of mitral stenosis with aortic insufficiency, the average height of the P wave was not much greater than that of uncomplicated mitral stenosis, and in no case it did exceed 5 mm. in amplitude, showing that disease of the aortic valve does not directly affect the amplitude of the P wave.

Duration of the P wave—Pardee (*loc. cit.*) has stated that the duration of the P wave is excessive being over 0·10 second in 85 per cent of the records of mitral stenosis. In this series the duration of the P wave exceeded 0·10 second in one lead or other in 44 cases (29·13 per cent). This is much below the percentage obtained by Pardee and others. This duration was increased in all the three leads in 3; in two leads in 18 and in one lead in 23 cases. Out of the 23 cases in which the duration was prolonged in one lead only, three were in lead I, one in lead II and nineteen in lead III. Instances of prolongation of the duration of the P wave over 0·10 second were found in all groups but they were most conspicuous in the group of mitral stenosis with failure of compensation. Alexander *et al* (1925) stated that the height of the P wave may be abnormally increased with little if any increase in duration, while the reverse is rarely true. We have found the same to be true in our records. An excursion that was wider than normal was associated in all instances with a P wave of an amplitude of 2 mm. and over; but an excursion which was higher than normal was not always associated with increased duration of the P wave.

Notching of the P wave—This was once regarded as a reliable indication of auricular hypertrophy. However, in later years various observers have independently observed its occurrence in a fair number of perfectly normal records. Lewis (*loc. cit.*) found notching in one lead or other in 32·7 per cent of 52 normal records. Shipley and Hallaran as quoted by Poynton and Schlesinger (1938) in 30 per cent of the 200, and Vakil (1941) in 38·5 per cent of 200 normal electrocardiograms. From the above observations it is clear that notching is one of the normal variations of the P wave. Pardee (*loc. cit.*) found that notching of the P wave occurs with unusual frequency, being observed in about 80 per cent of records from hearts with mitral stenosis and in only about 30 per cent of records from normals. In 151 cases in our series of mitral stenosis, uncomplicated or complicated with lesions of other valves with regular rhythm, notching was found in one or more leads in 33 cases (21·8 per cent). (*Fig. 5, 6 and 7*). The distribution of these 33 cases in the various groups is given in Table III. The occurrence of notching of the P wave in this study was much lower than its occurrence in normals. It will be seen from Table III that in only 10 per cent of the cases with mitral stenosis the P wave was notched. However, this percentage rises in the group of mitral stenosis with failure of compensation to 30, reaching its maximum of 40 in the group of mitral

stenosis and mitral insufficiency, and again drops to 26·8 in the group mitral stenosis and mitral insufficiency with failure of compensation. The distribution of notched P wave in the various groups suggests that notching is more likely to be produced when both auricles are enlarged than when only one auricle is affected as in most cases of mitral stenosis. It has been shown by Shipley and Hallaran as quoted by Poynton and Schlesinger (1938) and Hoskin and Jonescu (1940) that the association of the amplitude of P wave greater than 2 mm. and notching cannot be regarded as a normal variation as it did not occur even once in their records of the normals, and they considered this combination should suggest the existence of mitral stenosis. Vakil (*loc. cit.*) found this combination in a small percentage (3·1) of the normal records. The combination of a P wave of over 2 mm. with notching was noted in 31 (20·52 per cent) out of 151 cases of this series, and this association appears to be a much better indication of mitral stenosis than simple notching. Notching was not very conspicuous in P waves of large amplitude and it was found only in 6 out of the 36 cases in which P waves were over 5 mm.

Inversion of the P wave—Inversion of the P wave occurred in 16 out of the records of this series and that in lead III only. Lincoln and Nicolson (1928) observed splitting of R_3 or S_3 with inverted P_3 in normal children. Vakil (*loc. cit.*) found inverted P wave in lead III in 12·5 per cent of his normal cases. Prominent, broad, and notched P waves are usually seen in leads I and II and when associated with negative P in lead III denote mitral stenosis (Levine, 1940).

TABLE V—SHOWING DATA REGARDING INVERSION OF P WAVE.

		No. of cases	*Incidence of inverted P_3*
Group I	..	7	1
Group II (*a*)	..	51	4
(*b*)	..	17	0
Group III (*a*)	..	15	1
(*b*)	..	57	9
Group IV	..	11	1
		158	16

P-R INTERVAL (CONDUCTION TIME)

Prolonged P-R interval is very common in active rheumatic carditis but valvular lesions have little bearing on that interval. Levine (*loc. cit.*) made a correct diagnosis of acute rheumatic fever in a young girl of 13, suspected to be suffering from acute appendicitis by the electrocardiographic findings of prolonged P-R interval (0·3 seconds). This prolongation of P-R interval (auriculoventricular conduction time) that occurs in acute rheumatic infection is only temporary and disappears during convalescence. Excessive prolongation of the P-R interval is diagnostic of acute rheumatic infection provided syphilis is ruled out. This prolongation is abolished by the injection of atropine. The reduction in the P-R interval is observed as result of atropine, and over-stimulation of the vagus is the cause of this prolongation (Keith, 1938). The average value for P-R interval for normals according to Vakil (*loc. cit.*) taking all the standard leads into consideration is 0·148 second.

TABLE VI—SHOWING DURATION OF THE P-R INTERVAL.

	No. of cases	*P-R Interval (Average in seconds)*	*Incidence of prolonged P-R (No. of cases)*
Group I	7	0·12	Nil
Group II (*a*)	51	0·13	Nil
(*b*)	17	0·15	Nil
Group III (*a*)	15	0·14	1
(*b*)	57	0·14	Nil
Group IV	11	0·18	1
	158	0·14	2

It will be seen from Table VI that in 4 out of 6 groups the average was 0·14 second or lower. In two groups namely mitral stenosis with failure of compensation (Group II b) and mitral stenosis with mitral and aortic insufficiency (Group IV) the values were 0·154 and 0·181 seconds respectively. The maximum reading found in this series was 0·24 second and this occurred twice, once in the group of mitral stenosis and mitral insufficiency without failure of compensation (Group III a) and the other in the group of mitral stenosis, mitral and aortic insufficiency (Group IV). The percentage of cases showing prolonged P-R interval as observed by different authors vary from 4 (Bain and Hamilton, 1926) to 8·4 (Cohen and Swift, 1924) as quoted by Poynton and Schlesinger, 1937. The low figure of one per cent in our series can be accounted for only by the low incidence of acute cases. There were 36 cases in this series where the P-R interval was below 0·2 second but the interval was varying between 0·04 to 0·24 second.

TABLE VII—SHOWING DETAILS OF QRS COMPLEX

Group	*No. of cases*	*Incidence of Q wave* L I	L II	L III	*Duration of QRS. Average in sec.*	*Incidence of wide QRS (No of cases)*	*Amplitude of R wave in mm. (Average)*	*Incidence of R wave over 20 mm.*	*Incidence of S wave* L I	L II	L III
I ..	8	0	0	1	0·06	Nil	15·87	1	2	1	1
II (*a*) ..	54	0	2	10	0·06	Nil	14·24	Nil	23	17	10
(*b*) ..	17	0	1	1	0·07	Nil	13·25	Nil	12	3	3
III (*a*)	15	0	0	4	0·08	Nil	15·93	2	12	9	6
(*b*) ..	68	0	2	10	0·07	2	15·08	5	59	31	6
IV ..	11	2	3	2	0·08	Nil	15·50	Nil	3	6	7
	173	2	8	28	0·07	2	14·97	8	111	67	33

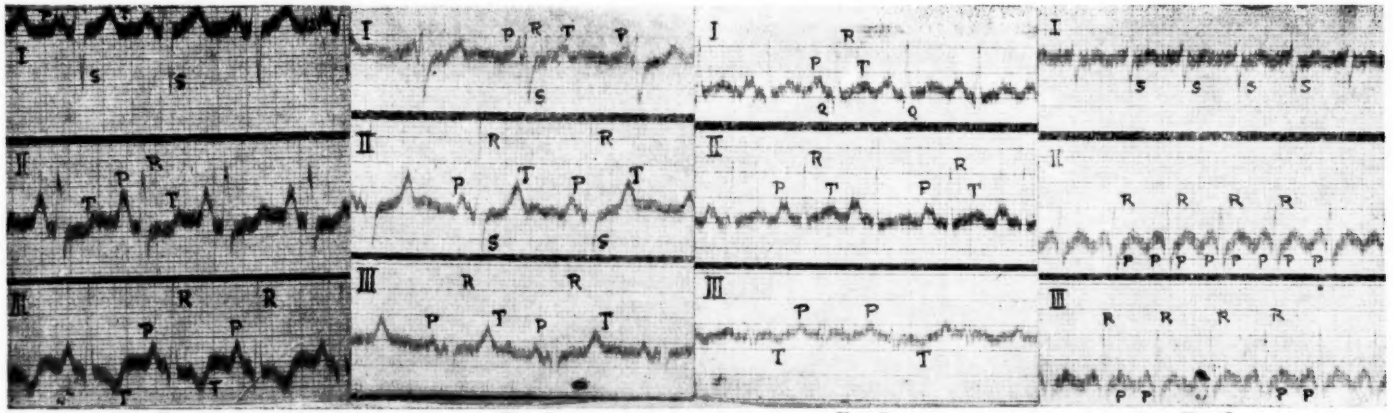

FIG. 5 FIG. 6 FIG. 7 FIG. 8

ABNORMALITIES IN P (AURICULAR COMPLEX) INCLUDING AURICULAR FLUTTER

FIG. 5. Leads I, II & III from a case of double mitral lesion. P is split in lead I. and prominent in leads II and III. Right axis deviation is present.
FIG. 6. Leads I, II & III from a case of double mitral lesion. P is split in leads I and II and biphasic in lead III. R and S are present in leads I and II.
FIG. 7. Leads I, II & III from a case of double mitral, with congestive heart failure. P is prominent and split in leads I and II. P-R 0·18 second, and Q is present in lead I.
FIG. 8. Leads I, II & III from a double mitral lesion showing auricular flutter (ratio 2 : 1).

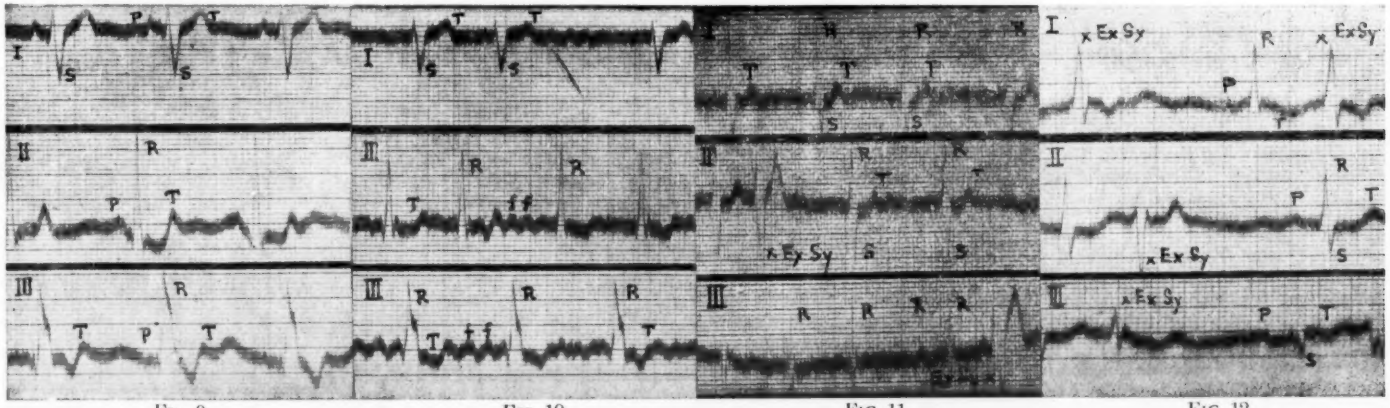

FIG. 9 FIG. 10 FIG. 11 FIG. 12

BUNDLE BRANCH BLOCK, AURICULAR FIBRILLATION AND EXTRA SYSTOLES

FIG. 9. Leads I, II & III from a double mitral lesion showing bundle branch block (right) in lead III.
FIG. 10. Leads I, II & III from the same case as above showing auricular fibrillation. Fibrillary waves are prominent.
FIG. 11. Leads I, II & III from a case of double mitral showing auricular fibrillation and ventricular extrasystoles in leads II and III.
FIG. 12. Leads I, II & III from the same case as in Fig. 7 showing pulsus bigeminus after administration of digitalis. P-R interval 0·2 seconds.

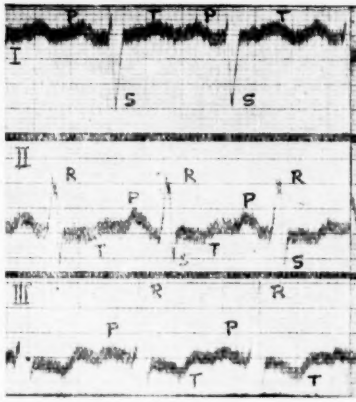

FIG. 13

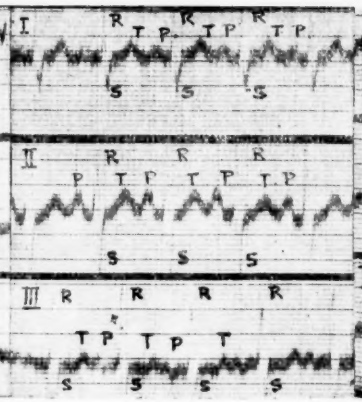

FIG. 14

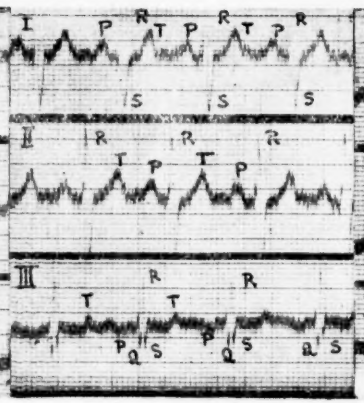

FIG. 15

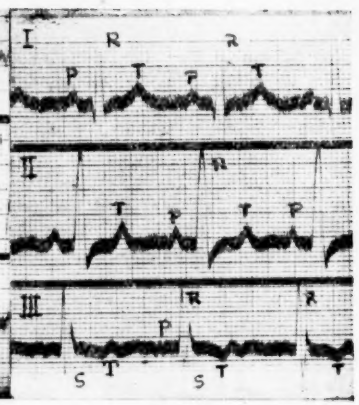

FIG. 16

ABNORMALITIES IN VENTRICULAR COMPLEX

FIG. 13. Leads I, II & III from a double mitral lesion showing splitting of R in lead II. S is present in lead II.
FIG. 14. Leads I, II & III from a double mitral lesion showing presence of R and S in leads I, II & III. P is split in lead I & II and negative in lead III. P is more prominent than T in lead II.
FIG. 15. Leads I, II & III from a double mitral lesion. In addition to the presence of R and S in leads I, II & III, Q is seen in lead III.
FIG. 16. Leads I, II & III from a case of rheumatic aortic regurgitation with involvement of the mitral valve, confirmed by post-mortem.

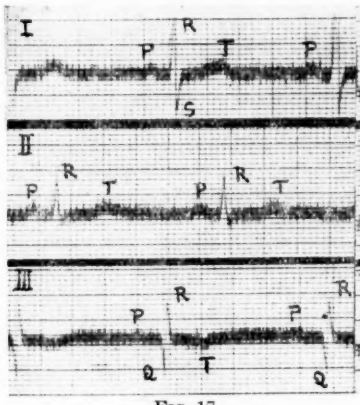

FIG. 17

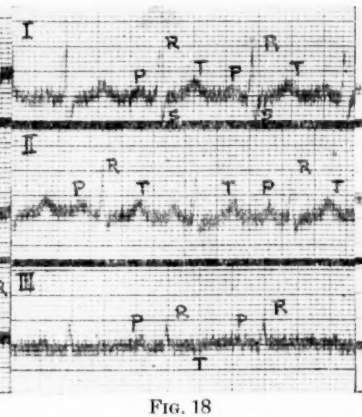

FIG. 18

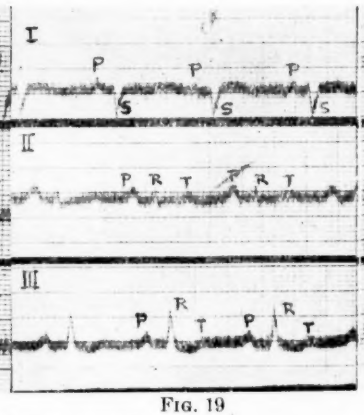

FIG. 19

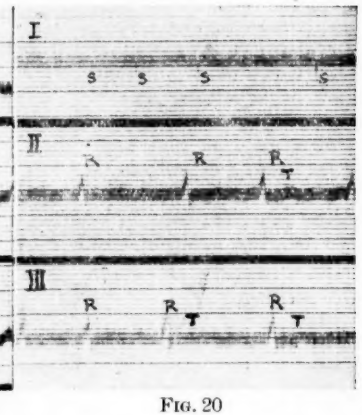

FIG. 20

MYOCARDIAL DAMAGE

FIG. 17. Leads I, II & III from a double mitral lesion showing the presence of Q in lead III.
FIG. 18. Leads I, II & III from the same case as above taken 3 weeks later showing the disappearance of Q. Low voltage in lead III.
FIG. 19. Leads I, II & III from a case of mitral stenosis, showing prolongation of P-R interval and low voltage in all leads.
FIG. 20. Leads I, II & III from a case of mitral stenosis, showing auricular fibrillation and low voltage in all leads.

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QRS Complex

Changes in the Q wave. Pardee (1930) has pointed out the significance of a large Q wave in the third lead. When found it was significant of a narrowing of a branch or branches of the coronary system and must have at least 25 per cent of the maximum excursion of QRS. Table VII gives the details with regard to the occurrence of the Q wave. In 30 cases, a Q wave was found either in one or more leads. In two cases it was found in lead I and in 8 cases in lead II and in 28 cases in lead III. There was no instance in which a Q wave was found in all the three leads. A Q wave measuring 25 per cent or more of the height of the R wave was found in two cases. In one the amplitude of Q 3 was 7 mm. and it was associated with a tendency to right ventricular preponderance. It was transient and disappeared in 3 weeks. (*Figs. 17 and 18*). In another case it was 8 mm. in amplitude and was associated with right ventricular preponderance. Pardee (1930) found large Q in 4 cases and small Q in 8 cases of rheumatic heart disease. The large waves were observed in one case of acute infection with mitral insufficiency, in 2 cases of aortic insufficiency with or without mitral disease and in one case of mitral stenosis. Small Q waves were observed in 3 cases of aortic insufficiency with or without mitral disease, in 2 cases of mitral insufficiency and in 3 cases of mitral stenosis with or without insufficiency.

Changes in the duration of the QRS complex. From a study of the duration of QRS in the various groups as is given in Table VII it would appear that mitral valvular disease as such has little influence on the interventricular conduction. The average value of the QRS interval in normals for the standard leads is 0·073. There were two cases of right bundle branch block in this series. In both cases the duration was 0·12 seconds (*Fig. 9*) and they occurred in the groups with mitral stenosis and mitral insufficiency with failure of compensation. Aortic insufficiency often produces an increase in the duration of the QRS but in this series there was not a single case in which the duration exceeded 0·10 second. Splitting of QRS complex occurred in 11 cases; in lead I alone, 1 case; in lead II alone, 3; in lead III alone, 5; in leads I and II one case and in lead II and III one case.

Ventricular Preponderance—Different authorities have laid down different criteria for ventricular preponderance which is rather confusing. We have followed the criteria suggested by Berliner and Master (*loc. cit.*). A diagnosis of right ventricular preponderance was made when lead I had no R wave or but a small one, with the downward deflection, with S larger than R; and in addition R_3 had to be taller than R_2. Diagnosis of left ventricular preponderance was made when lead III had no R wave or only a small one, with S larger than R; in addition R_1, had to be taller than R_2. A tendency to right ventricular preponderance was diagnosed when there was a low R wave in lead I, with S larger than R_1 but R_3 not taller than R_2. A tendency to left ventricular preponderance was diagnosed when there was a low R wave in lead III. with S larger than R but with R_1 not taller than R_2. Table VIII gives the data with regard to ventricular preponderance. In Group I there was no case in which ventricular preponderance was noted. In 82 cases *i.e.*, 52 per cent of mitral stenosis, mitral stenosis and insufficiency with or without failure of compensation, there was either right ventricular preponderance or a tendency to it. The percentage distribution of these cases in the first three groups (including II b, and III b) is instructive and it was 0, 18·5, 64, 66 and 72 respectively. Berliner and Master (*loc. cit.*) by a correlation of electrocardiographic and pathologic observations have found that right ventricular preponderance depends on the degree of stenosis. The tighter the stenosis the more definite the right ventricular preponderance. A study of the relative amplitudes of the R and S waves in the three standard leads gives valuable information as to the degree of the ventricular preponderance. In 16 out of the 59 cases of right ventricular preponderance R_3 was equal in height to R_2; in 21 cases, in addition to S_1, S_3 was present and in 7 cases S wave was present in all the three leads. Pardee has lucidly explained the significance of an R_3 which is equal to R_2 and the presence of S_2 and S_3. If R_2 and R_3 are equal it indicates an electrical axis on the borderline of normal. As the degree of right axis deviation increases S_1 gradually increases until it equals R_3 or even exceeds it. Similarly in left axis deviation, as the axis deviation increases, S_3 increases until it becomes equal to R_1 or even exceeds it. S_2 might be part of a record showing either right or left axis deviation and without other leads we cannot say which it is. When S_3 gives the greatest amplitude and S_2 approaches the size of R_1 we have an extreme grade of left axis deviation. Unlike in right ventricular preponderance where an S_3 is of common occurrence, in left ventricular preponderance an S_1 rarely occurs. In 48 per cent of the cases associated with mitral stenosis and mitral stenosis and insufficiency with or without failure of compensation, there was no eivdence of any ventricular preponderance. In these cases it is to be inferred that the mitral stenosis has not reached a magnitude to influence the weight of the right over the left ventricle. In Group IV of mitral stenosis, mitral and aortic insufficiency, there were three cases of left ventricular preponderance and 2 cases of a tendency to left ventricular preponderance and two cases of right ventricular preponderance. Three cases showed no ventricular preponderance. In the remaining one case an earlier electrocardiogram showed right ventricular preponderance and later one showed a change to left ventricular preponderance. Berliner and Master (*loc. cit.*) found that ventricular preponderance depended on the extent of the aortic leak. Tight mitral stenosis complicated by a moderate aortic insufficiency often was associated with right ventricular preponderance. In all the cases of marked aortic insufficiency with high pulse pressure, however, there was left ventricular preponderance whether the associated mitral stenosis was slight or marked. Associated lesions of the tricuspid valve tend to swing the

TABLE VIII—SHOWING DATA REGARDING THE OCCURRENCE OF VENTRICULAR PREPONDERANCE

Group	*No. of cases*	*Tendency to V.P.R.*	*V.P.R.*	*Tendency to V.P.L.*	*V.P.L.*
I	8	Nil	Nil	Nil	Nil
II (*a*)	54	9	1	Nil	3
(*b*)	17	5	6	Nil	Nil
III (*a*)	15	3	7	Nil	1
(*b*)	68	4	45	2	1
IV	11	Nil	2	Nil	3
	173	21	61	2	8

balance of the ventricles towards right ventricular preponderance. Mitral insufficiency generally has a less marked effect on ventricular preponderance. If it is very marked it may swing the balance of the ventricles towards left ventricular preponderance.

Voltage of QRS—Pardee (*loc. cit.*) has stated that many patients with marked mitral stenosis have large excursions of QRS and he has attributed the increased size of the deflection to cardiac hypertrophy. But Berliner and Master (*loc. cit.*) found that in not one of their 19 cases of uncomplicated disease of the mitral valve was the QRS complex higher than 16 mm.. the upper limit for the normal as observed by Pardee. They further observed that the degree of stenosis did not affect the voltage of the QRS at all, the normal voltage of the QRS being 5 to 20 mm. in the lead showing the highest excursion. There were 16 cases in which the excursion of the R was 20 mm. and 8 in which the excursion was more than 20 mm. The highest amplitude encountered was 32 mm. Of the 8 cases one occurred in Group I, 2 in Group III (a) (mitral stenosis and mitral insufficiency without failure of compensation) and the remaining 5 in the group III(b) (mitral stenosis and insufficiency with failure of compensation. In all the 8 cases there was right ventricular preponderance in this series. Vakil found the average amplitude of R in lead II, the lead showing the highest excursion in normal electrocardiogram, to be 12 mm. and the range 2·9 to 25·2 mm. and the average amplitude of R in records showing right ventricular preponderance was 15·5 mm. and the range was 4 to 32 mm. In 21 cases which showed a tendency to right ventricular preponderance the average excursion of the R in lead II was 14·72 mm. and the range 8 to 20 mm. The average excursion of the R for the cases showing no ventricular preponderance was 13·87 and the range from 1 to 22 mm. From this it is seen that the amplitude of the R is influenced by mitral stenosis and the range of the excursion is greatest in cases where there is marked right ventricular preponderance. There was a progressive increase in the averages of the amplitude of the R from cases of mitral stenosis with no ventricular preponderance, to mitral stenosis with a tendency to right ventricular preponderance to mitral stenosis with pronounced right ventricular preponderance the average being 13·87 mm. 14·72 mm. and 15·5 mm. respectively all of them well above normal. They have further noted that the presence of aortic insufficiency had a marked effect on the voltage of QRS and the highest excursions were found in these cases. This statement is not borne out by our study. In this series there were 8 cases in which mitral stenosis in association with aortic regurgitation was noted and in which either a left ventricular preponderance or a tendency to left ventricular preponderance was noted. The average excursion of the R in these cases was 13·3 mm., a little less than the average for mitral stenosis and regurgitation in which no ventricular preponderance was noted. The voltage of the electrocardiogram is no indication of the size of the ventricle and there is no constant relation between the height of the QRS complex and the degree of ventricular hypertrophy. There were two cases in this series in which low voltage of the QRS complex was noted. One of these occurred in the mitral stenosis group and was associated with auricular fibrillation (Fig. 20). The highest excursion of the R wave was 3 mm. The other one occurred in the group of mitral stenosis and insufficiency with failure of compensation. This was associated with nodal rhythm, and the highest excursion of the R wave was 4 mm.

S-T Interval

The average value for S-T interval in normals according to Vakil (1941) is 0·26 seconds, taking all the 3 leads into consideration. The average value for the S-T duration in the various groups were, mitral stenosis 0·244; mitral stenosis with failure of compensation 0·244; mitral stenosis with failure of compensation 0·240; mitral stenosis and insufficiency 0·261; mitral stenosis and insufficiency with failure of compensation 0·241 and mitral stenosis and mitral and aortic insufficiency 0·250 seconds. Rothschild *et al* (1927) as quoted by Poynton and Schlesinger, 1937, considered an elevation of S-T interval above the iso-electric line in one or more leads as evidence of myocardial involvement in acute rheumatic fever of adults. Shapiro (1930) quoted by Poynton and Schlesinger, 1937, in his study of electrocardiographic changes in quiescent rheumatic disease in children and young adults found that many of the tracings showed changes similar to those found in acute rheumatic fever.

In this series there were five cases in which an abnormality of the S-T interval was noted. In four of these cases this was depressed below and in one it was elevated above the iso-electrical line in L II and L III. In 3 of the 4 cases in which the S-T interval was depressed an associated alteration in the P-R interval was noted and it was found to be varying. The intervals were 0·08 to 0·12; 0·16 to 0·20 and 0·12 to 0·16 seconds respectively. In the instance where the S-T interval was elevated there was a small Q in lead II but it was very much less than 25 per cent of the largest QRS deflection.

There was no right ventricular preponderance and the P-R interval was lengthened to 0·24 second.

Changes in the T Wave

Details with regard to T wave is given in Table IX.

Table IX—Showing Details with regard to T Wave

Group	No. of cases	T 1				T 2				T 3			
		Negative	Zero	Positive	Biphasic	Negative	Zero	Positive	Biphasic	Negative	Zero	Positive	Biphasic
I ..	8	—	—	8	—	—	—	8	—	3	2	3	—
II (*a*) ..	54	—	3	51	—	3	3	46	2	17	8	29	—
(*b*) ..	17	1	1	15	—	3	3	13	1	7	2	8	—
III (*a*) ..	15	—	—	15	—	—	—	12	2	7	2	6	—
(*b*) ..	68	—	8	60	—	19	19	44	2	35	9	40	4
IV ..	11	2	—	9	—	—	—	10	1	5	—	5	1

Taking all the leads into consideration 42 cases showed definite abnormalities in the T wave. The details are given below:—

Group II (*a*)	Negative L II, L III—3 cases	
	Biphasic L II, Negative L III—2 cases	
	Zero L II, Negative L III—2 cases	
	Zero L I, Zero L II, Negative L III—1 case	8
(*b*)	Negative L II, L III—2 cases	
	Zero L I, Negative L II, L III—1 case	
	Biphasic L II, Negative L III—1 case	4
Group III (*a*)	Zero L II, Negative L III—1 case	
	Biphasic L II, Negative L III—1 case	2
(*b*)	Negative L I, L II, L III—1 case	
	Zero L I, L II, L III—2 cases	
	Zero L I, Negative L II, L III—1 case	
	Negative L II, L III—17 cases	
	Zero L II, Negative L III—1 case	
	Biphasic L II, Negative L III—2 cases	
	Biphasic L II, L III—2 cases	26
Group IV.	Negative L I, Positive L II, L III-1 case	
	Negative L I, Biphasic L II, L III-1 case	2

Gross abnormalities as negative or zero T in all the three leads were seen in 5 cases. In one case low voltage was present in all the leads and electrocardiogram showed in addition regular sinus rhythm, varying P-R interval and right ventricular preponderance. The second case showed sinus arrhythmia, small Q in L III, prolonged S-T interval, right ventricular preponderance and low voltage in all the three leads. This patient died 15 days after the electrocardiogram was taken. The third case showed auricular fibrillation with right ventricular preponderance, and fibrillary waves were prominent. The fourth case showed regular sinus rhythm, P-R interval in the maximum limit (0·2 second) and right ventricular preponderance. The last case showed only regular sinus rhythm and split QRS in lead III.

Master (1935) has shown that inversion of T_3 or both T_2 and T_3 is commonly associated with marked enlargement of the right ventricle whereas inversion of T_1 or T_1 and T_2 is commonly associated with enlargement of the left ventricle. In 15 instances a negative T_2 and T_3 was associated with right ventricular preponderance and in two instances with a tendency to right ventricular preponderance. In another 22 instances negative T_3 was associated with right ventricular preponderance and in 14 instances with a tendency to right ventricular preponderance. Thus out of 82 instances of right ventricular preponderance and tendency to right ventricular preponderance in this series, 53 cases showed a negative T wave either in lead III or in lead II and III together. In 8 cases in which left ventricular preponderance was noted in 2 cases the T_1 was negative in association with left ventricular preponderance or a tendency to left ventricular preponderance close relationship or association was observed between the P and the T waves by Hoskin and Jonescu (*loc. cit.*) and by Shipley and Hallaran (*loc. cit.*). Inverted P meant inverted T and biphasic P meant biphasic T. A study of our records do not confirm their observations. In the 16 records in which the P_3 was inverted, in only 6 the T_3 was inverted. There were two cases in which the P_3 was biphasic and in these the T_3 was positive.

Cardiac Arrhythmias

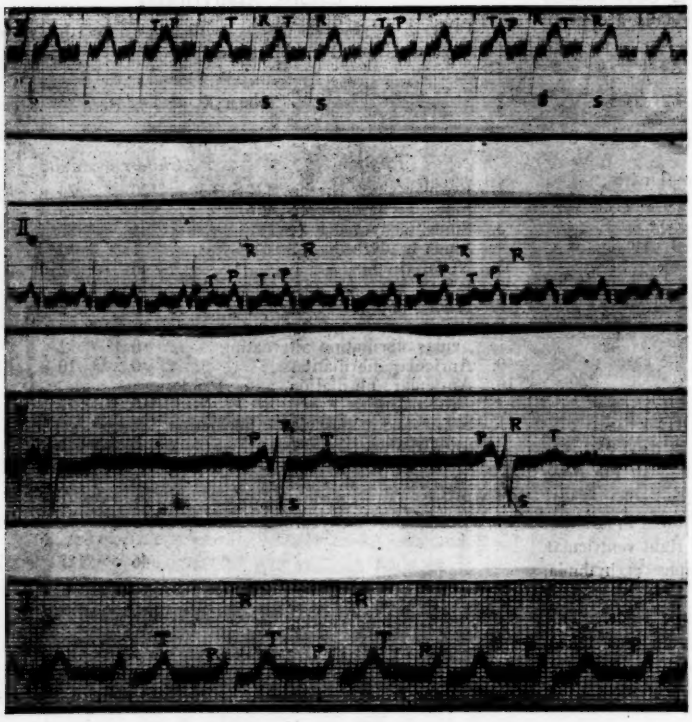
Table X gives the details with regard to the varieties of arrhythmias noted in this series.

Table X

	Rhythm	*Children*	*Adults*	*Total*
1.	Regular sinus rhythm (R.S.R.) ..	20	74	94
2.	Sinus arrhythmia (S.A.) ..	1	3	4
3.	Sinus tachycardia (S.T.) ..	23	27	50
4.	Sinus bradycardia (S.B.) ..	1	0	1
5.	Nodal rhythm	0	2	2
6.	R.S.R., S.T. and S.B. alternating ..	0	2	2
7.	R.S.R. and S.T. alternating ..	0	2	2
8.	R.S.R., auricular flutter and auricular fibrillation alternating ..	0	2	2
9.	Auricular fibrillation	0	10	10
10.	Auricular fibrillation and R.S.R. alternating	0	1	1
11.	S.T. and auricular fibrillation alternating	0	1	1
12.	S.A., R.S.R., S.T. and auricular fibrillation alternating ..	0	1	1
13.	R.S.R. and S.B. alternating ..	1	1	2
14.	Ventricular tachycardia ..	0	1	1
		46	127	173

Regular sinus rhythm was present in 94 cases and sinus tachycardia (*Figs. 1 and 2*) in 50 cases, the rate varying from 100 to 192 per minute. Sinus arrhythmia was seen in 4 cases only, in the records. Clinically more cases showed this arrhythmia but it was not reproduced in the electrocardiogram. Auricular fibrillation occurred with sinus tachycardia, regular sinus rhythm and sinus arrhythmia at different periods and at varying intervals in 3 cases. Two cases of auricular flutter (*Fig 8*) were noted in this series and these passed on to auricular fibrillation and normal rhythm was restored during intervals. Nodal rhythm (*Fig. 4*) occurred in two cases. In one of these cases that showed multiple arthritis the heart did not show any clinical evidence of rheumatic infection but the electrocardiogram showed that the cardiac muscle was involved as shown by the nodal rhythm. Sinus bradycardia (*Fig. 3*) occurred with regular sinus rhythm at intervals in two cases. In a review of 39 cases of auricular fibrillation in Indian subjects, Raman (1937) found only one case below 20 years and the patient was aged 19. In a study of 150 cases of rheumatic heart disease in children below 16 years of age Kutumbiah (1941) did not find a single case of auricular fibrillation.

Sinus tachycardia is commonly observed, sinus bradycardia is an occasional feature, sinus arrhythmia is observed and its presence does not indicate that the heart muscle has escaped; nodal rhythm occasionally occurs, auricular flutter is not common and auricular fibrillation is common in chronic infections but rare in childhood, (Poynton and Schlesinger, 1938). Coombs (1924) pointed out the rarity of auricular fibrillation below the age of 20 years. Cookson (1929) reported 30 cases of auricular fibrillation in children due to rheumatic infection from a series of 1164 cases of auricular fibrillation admitted in the London Hospital during a period of 15 years.



ABNORMALITIES IN THE CARDIAC RHYTHM

FIG. 1—Lead II from a case showing sinus tachycardia.
FIG. 2—Lead II from another case showing sinus tachycardia.
FIG. 3—Lead II from a case showing sinus bradycardia occurring with regular sinus rhythm.
FIG. 4—Lead II from a case showing nodal rhythm.

EXTRA-SYSTOLES

Table XI gives the varieties of extra-systoles noted in this series.

TABLE XI—SHOWING THE VARIETIES OF EXTRA-SYSTOLES

Extra-Systoles			
1. Auricular (alone)			Nil
2. Ventricular			
(*a*) Right L I and L II	1		
L II and L III	1		
L I, L II and L III ..	1		3
2 cases alternated with auricular fibrillation.			
(*b*) Left L II	1		
L I and L II	1		
L II and L III	1		3
Last case associated with auricular fibrillation.			
(*c*) Right and left			1
3. Auricular and ventricular L II			1
4. A.P.C., L II, V.P.C., L I, L II, L III			1
5. Nodal, interpolated and ventricular			1
6. Ventricular trachycardia			1
Total			11

Extra-systoles occurred in 11 instances only. All the cases were chronic. Of these only two were induced by digitalis. Raman (1940) from a study of 41 cases of extra-systoles found that 11 cases (25 per cent) were rheumatic in origin. Extra-systoles occurring in acute rheumatic infection are probably the result of active myocarditis and often persist in children for many years (Poynton and Schlesinger, 1938).

Table XII gives the incidence of extra-systoles in rheumatic infection as given by different authors:

The fact that the number of acute cases were few and some of the extra-systoles observed at the bedside could not be recorded in the electrocardiogram will explain the low incidence observed in our series.

Ventricular tachycardia occurred in a young girl of 19 years as a result of digitalisation. Short paroxysms appeared in the earlier stages (*Fig. 21*); later, longer paroxysms occurred (*Fig. 22*) and the patient died about three weeks after discharge from the hospital.

DISCUSSION

The question is often asked whether the electrocardiogram is of any help in the diagnosis of valvular disease of the heart. Until the valvular lesion progresses to such a degree as to produce marked anatomic changes in the heart no deviation from the normal type of electrocardiogram could be expected. The most common changes that result from a valvular lesion are dilatation and/or hypertrophy of the chambers of the heart. When these occur they produce definite deviation from the normal electrocardiogram. Various types of electrocardiograms have been described as characteristic of certain valvular lesions. The most important of these types is "the mitral type" of electrocardiogram. Our study reveals that the amplitude of P wave was greater than normal in 50 to 80 per cent in different groups, broad P wave in 29·13 per cent notching in 21·8 per cent right ventricular preponderance and in 52 per cent of the cases in which a clinical diagnosis of mitral stenosis was made. These findings suggest that the combination of a P wave of a larger amplitude than normal and right ventricular preponderance is characteristic of the electrocardiogram of mitral stenosis. If at the same time the P wave is broader than normal and it is notched then the picture is complete. But this combination occurred in 8·6 per cent of the cases of mitral stenosis only, whereas the combination of the P wave of greater amplitude than normal and right ventricular preponderance occurred in nearly 37 per cent of the cases. Our study does not confirm the observation of Berliner and Master that notching of P wave definitely remains the most character-

istic electrocardiographic sign of mitral stenosis. They further remark that if there is a marked right ventricular preponderance and at the same time the notched P wave is very high and wide, the presence of an associated tricuspid lesion may be safely assumed. In tricuspid stenosis no diagnostic significance can be attached to the electrocardiogram (Cook and White, 1941). In the only case of tricuspid and mitral stenosis diagnosed clinically, the P wave in lead II was 6 mm. in amplitude but it was neither notched nor wider than normal. There was an associated right ventricular preponderance. Our study shows that notching was relatively more common when both the auricles were enlarged and this enlargement might be due either to a tricuspid insufficiency or stenosis or both. Without the physical signs, a diagnosis of tricuspid stenosis on electrocardiographic records alone is not justified. In 48 per cent of the cases clinically diagnosed as mitral stenosis no marked alterations in the auricular complex in the electrocardiogram were noted. A mitral type of electrocardiogram confirms a diagnosis of mitral stenosis but its absence does not rule out its presence. Aortic insufficiency as our analysis shows, produces either left or right ventricular preponderance. In mitral stenosis it is rare to come across a left ventricular proponderance. When this occurs in a mitral type of electrocardiogram the possibility of a coexisting aortic leak must be considered. The production of right ventricular preponderance in

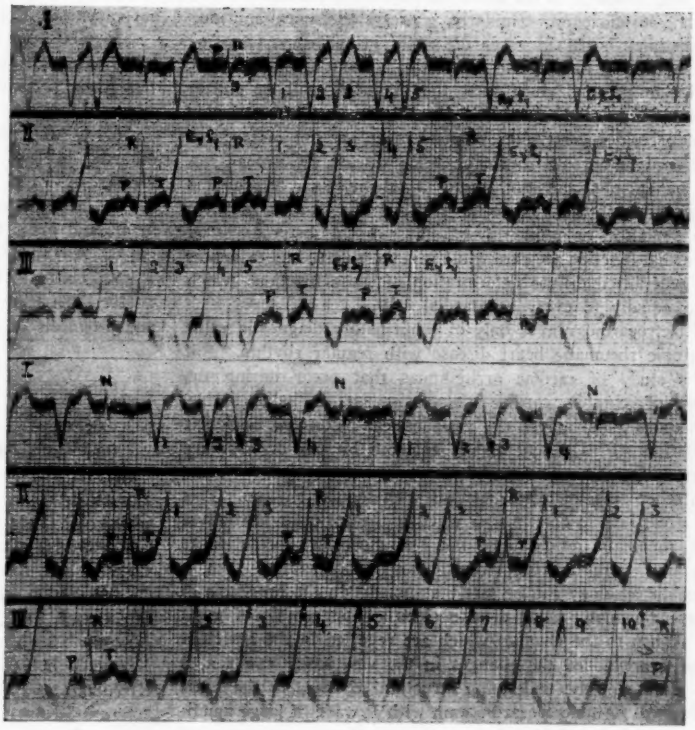


FIG. 21

FIG. 22

FIG. 21—Leads I, II and III from a case showing ventricular tachycardia (as a result of digitalisation) with short paroxysms appearing in the earlier stage.

FIG. 22—Leads I, II and III from the same case showing longer paroxysms occurring in the later stage.

TABLE XII

Observers.	*No. of cases.*	*Auricular extra systoles.*	*Ventricular extra systoles*	*Nodal extra systoles*	*Combined. (Auricular, Nodal, Ventricular & Interpolated.)*	*Total incidence.*
Parkinson *et al* (1919) ..	50	7	3	2	—	24%
Cohn & Swift (1924) ..	37	10	10	2	—	62%
Reed & Kunway (1928) .. (Quoted by Poynton & Schlesinger)	26	3	3	3	—	34%
Kutumbiah & Raman (Present series)	173	—	9	—	2	7%

cases of aortic insufficiency and mitral stenosis depends on the relative degrees of the mitral stenosis and the aortic leak. If the mitral stenosis is tight and the aortic leak small then right ventricular preponderance is produced. If on the other hand, the aortic leak predominates left ventricular preponderance results. This changes from a right to left ventricular preponderance or *vice versa* is much more characteristic of combined mitral, aortic and tricuspid lesions, according to Berliner and Master. The occurrence of left ventricular preponderance in a suspected case of mitral stenosis is of great practical importance in the differential diagnosis of certain murmurs which occur during the course of mitral or aortic disease. In oldstanding cases of mitral stenosis a diastolic murmur (Graham-Steel murmur) best heard in the third intercostal space close to the left border of the sternum often occurs. Both in character and distribution it is indistinguishable from the diastolic murmur of aortic insufficiency. If this murmur is associated with a left ventri-

cular preponderance in the electrocardiogram, the diagnosis will be aortic insufficiency. Similarly, a presystolic apical murmur is sometimes heard in cases of aortic insufficiency (Austin-Flint murmur) and if the electrocardiogram shows a right ventricular preponderance then the diagnosis will be mitral stenosis. Our study reveals that changes in the ventricular complex besides ventricular preponderance are not of frequent occurrence in chronic rheumatic heart disease. Coombs (*loc. cit.*) has pointed out that there is seldom such a profound deterioration of the ventricular wall in this disease as there is in syphilitic or senile myocarditis. Focal disturbances of myocardial function are rare while it is the rule to find evidences of a generalised diffuse deterioration of those functions which belong equally to every myocardial cell.

Electrocardiogram is only of confirmatory diagnostic value in chronic rheumatic heart disease with regular rhythm. But in the study of cardiac arrhythmias that occur during the course of chronic cardiac rheumatism it is indispensable. Electrocardiogram gives the most typical picture of auricular fibrillation. P is absent and is replaced by (f) or fibrillary waves (*Fig. 10*). The ventricular complex remains the same as in other cases of mitral stenosis with regular rhythm. This is of great help in determining whether the auricular fibrillation is of rheumatic ætiology or not. If auricular fibrillation is associated with a right ventricular preponderance then a rheumatic ætiology can be safely assumed. In the prognosis of chronic rheumatic heart disease electrocardiogram is of great aid. When to the changes which are revealed in the auricular complex are added the changes in the ventricular complex, a true picture of the underlying structural changes in the heart is obtained. An electrocardiogram with P wave of large amplitude, notched in all the three leads and broader than normal with marked right ventricular preponderance shows a marked mitral stenosis. The existence of auricular fibrillation in association with right ventricular preponderance denotes a further damage to the cardiac muscle. Any lengthening of the Q R S interval, a large Q in lead III, elevation of the S-T interval over the isoelectric line and an electrocardiogram of low voltage all point to marked structural damage of the myocardium.

Summary

1. Electrocardiograms of 173 cases of rheumatic heart disease treated in the King George Hospital, Vizagapatam, are analysed.

2. All these cases were in Indians and the greatest incidence was betwen 15 and 25 years.

3. Changes in the P (auricular complex) such as amplitude duration, notching and inversion are described and their significance discussed.

4. Prolongation of P-R interval occurred only in 2 cases but varying P-R interval occurred in 20 cases.

5. Sixty one cases showed right ventricular preponderance and 8 cases left ventricular preponderance. The significance of ventricular preponderance in chronic rheumatic heart disease is discussed.

6. Q was present in 38 cases in different leads but 28 occurred in lead III. Bundle branch block was present in 2 cases.

7. Mild degrees of abnormality in T waves were observed in 42, and gross changes in 5 cases.

8. All varieties of cardiac arrhythmias were observed.

9. Extra systoles occurred in 11 (7 per cent) cases.

10. The significance of electrocardiogram in the diagnosis and prognosis of rheumatic disease is discussed.

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DR. K. S. RAY GOLD MEDAL FOR PAPER ON PUERPERAL SEPSIS

It is announced for information of the medical profession that the last date for receipt of papers on Puerperal Sepsis containing a record of original work and investigation on the subject for which a gold medal will be awarded by Dr. K. S. Ray, as ex-President of the Indian Medical Association, to the best worker at the next Session of the All-India Medical Conference to be held in Cawnpore during the coming Christmas holidays will be the 30th November, 1943. Research workers and investigators who intend to submit a record of their work on this subject are requested to send six typed copies of their articles to the undersigned so as to reach him by the 30th November, 1943.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

23. Hindusthan Buildings,
Calcutta.

MALARIA

A PRELIMINARY REPORT ON THE STUDIES ON THE ACTION OF 'ABN-61' (A PREPARATION OF DITA-BARK & QUININE) ON CASES OF HUMAN MALARIA

B. C. ROY, B.A., M.D. (CAL.), F.R.C.S. (ENG.), M.R.C.P. (LOND.).
Director, Sir Nilratan Sircar Research Institute; Physician, Carmichael Medical College Hospitals, Belgachia, Calcutta
AND
K. D. CHATTERJEE, M.D. (CAL.),
Clinical Tutor, Department of Medicine, Carmichael Medical College Hospitals, Belgachia, Calcutta.

General Consideration

Malarial fevers are caused by a protozoal parasite belonging to the class Sporozoa, suborder Hæmosporidia, genus plasmodium. There are three main species of malarial parasites which infect man. They include the following:—*Plasmodium vivax* (Grassi & Feletti, 1890) causing benign tertian malaria, *plasmodium falciparum* (Welch, 1897) causing malignant malaria, *plasmodium malariæ* (Laveran, 1881) causing quartan malaria. These species are widely distributed in the tropics. *Plasmodium ovale* (Stephens, 1922) is a rare species and was mainly reported from Africa. It should be noted that besides man, birds and monkeys are also parasitised by various species of plasmodia some of which include the following:—*plasmodium relictum* (præcox) in sparrows, *plasmodium gallinaceum* in fowls, *plasmodium knowlesi* in Simian monkeys.

Inoculation of *plasmodium knowlesi* in man can give rise to fever of mild type with a tendency to spontaneous cure. This species of parasite has recently been introduced for malaria therapy in dementia paralytica (general paralysis of insane). Further, the parasites of bird malaria and monkey (Simian) malaria are being extensively used in the experimental work on malaria.

So far as the human plasmodia are concerned, they pass their life cycle in two different hosts. The one called asexual cycle (Schizogonous) is passed in man (intermediate host) and the other called the sexual cycle (gametocytic) is passed in certain types of female anopheline mosquitoes.

When gametocytes are only found, they indicate that the man is a carrier.

The view that the parthenogenesis of gametocytes may explain the cause of relapse is not accepted. These gametocytes are infective to a female anopheline mosquito and if not taken by these insects they live only for a period of 20 to 40 days, after which they undergo spontaneous degeneration, even without any treatment.

Parasiticidal Action of Quinine

The parasiticidal action of any specific drug depends on the rate of parasitic multiplication and the rate of parasitic destruction. The schizogony cycle of various species of malarial parasites and the number of merozoites formed by each are shown below:—

Plasmodium vivax—16 to 24 merozoites every 48 hours; produces paroxysm every third day; not easily destroyed by quinine.

Plasmodium falciparum—28 to 32 merozoites every 48 hours or under; produces paroxysm every 36 or 48 hours; most influenced by quinine.

Plasmodium malariaæ—6 to 12 merozoites events 72 hours; prduces paroxysm every fourth day; refractory to quinine.

The specific action of antimalarial drugs, like quinine and atebrin, brings down the parasitic count of all species of human plasmodia to a sub-clinical level which is unable to cause any febrile paroxysm. These specific drugs also have a destructive action on gametocytes of *pl. vivax* and *pl. malariæ* but are unable to kill the gametocytes of *pl. falciparum*. The only drug which has a destructive action on these gametocytes is 'Plasmochin'.

Relapses are frequent in malarial infections. This is due to the fact that after the fever subsides, the parasites disappear from the peripheral circulation and retire as it were, to some internal organs where they continue to exist. In such a case, the number is insufficient to cause symptoms or to be detected by ordinary laboratory methods of examination. The first relapse usually appears about 3 to 4 weeks after the initial attack has ceased, when the parasite reappears in the peripheral blood. Relapses tend to occur even with specific remedies like quinine and atebrin. Liability to relapse varies with different species of parasites. With *pl. vivax* it has been found to last upto 3 years from the time of the original infection, with *pl.* malariæ upto 6 years; and with *pl. falciparum* upto 9 to 18 months. Relapses occurring after a long interval should be differentiated from cases arising from re-infection, which, however, is not always possible to be verified, or eliminated.

History of Malaria Therapeutics

The parasite of malaria was discovered by the French military surgeon, Alphonse Laveran in 1880 and it took another 18 years when Sir Ronald Ross in 1898 established the mosquito transmission theory. But the treatment of malaria with cinchona bark was known long before the etiology of the disease was discovered. The story of a specific remedy for malaria with quinine starts from the year 1630 when the Countess del Chinchon, wife of a Spanish Viceroy of Peru was cured of 'ague' (malaria) by a native bark. Linnaeus in about the year 1740 named the tree as cinchona in honour of the Countess. The Peruvian bark was subsequently introduced in Europe by the Jesuits in the first half of the 17th century. Later in the first quarter of the 19th century, Pelletier and Cavantou (1820) isolated the principal alkaloid 'quinine' from the cinchona bark. The name 'quinine' is said to be derived from 'quina' the spanish way of spelling the Peruvian word 'kina', that is, bark. For a long time quinine and other allied alkaloids held the field of specific antimalarial therapy.

Researches proceeded on to find out a stronger and better substitute for quinine and it was the last war of 1914-1918 which gave an impetus to German chemists like Professor Schuleman and his colleagues to synthesise a product from methylene blue to supplement the natural alkaloid quinine. It was in September 1926 that they announced a product called 'Plasmochin' and its efficiency was tested by Rohel against bird malaria. 'Plasmochin' was an expensive drug and the hope that it would replace cinchona alkaloids as an antimalarial remedy was not met with great success, because of its feeble action on the

schizogony cycle of *falciparum*. The only striking effect of this drug which superseded all other antimalarial remedies so far discovered, was its destructive action on the gametocytes of *pl. falciparum* and in this respect it is even superior to quinine. Six years after the discovery of 'Plasmochin' another new compound, also a derivative of methylene blue, 'Atebrin' was obtained by Mauss and Mietzsch. This synthetic product, first named 'Erion' was found effective against bird malaria by Kikuth in 1932. This drug acts powerfully on all species of malarial parasites and compares favourably with quinine, but like the latter drug it is ineffective against gametocytes of *pl. falciparum*. Recently other synthetic antimalarials like Certuna by Kikuth and Ciliqnal by Schuleman have been prepared.

Quinine in Malaria

For over 300 years the alkaloids of cinchona bark were without any competition as specific in malaria and even today. quinine stands as the foremost remedy against malaria. The quinine problem of the province, as well as of India has assumed a great dimension during the present war. The Official Report of 1939 showed that the annual consumption of quinine in India was 210,000 pounds of which, 70,000 pounds were produced locally and for the balance, India had to depend on foreign import. But the annual requirements are really greater. It has been mentioned on a conservative estimate that about 100 million persons in India suffer from malaria in each year and therefore, the annual requirement of quinine for the purpose of effective mass treatment will amount to 1,200,000 pounds (calculating on the basis of 90 grains to each patient), that is, about six times the present yearly consumption. But even then one has to consider the question of relapses. Besides this, whenever there is a possibility of a widespread outbreak of malaria throughout the country (as happened recently during and following famine conditions in Bengal), the amount of quinine requirement will be increased still further.

With limitations of foreign import, the country has to depend mainly on her own production. Although the present production is somewhat over 90,000 pounds and even if the State desires to increase the production of cinchona plantation, it will take a number of years (8 to 10 years) to raise the quinine output so as to make the country self-sufficient. Under the present circumstances the continued demand on quinine as a specific antimalarial remedy when no other specifics like atebrin (mepacrine) and plasmochin (pamaquine) are available, will greatly reduce the quinine stock of India. Some firms have undertaken the manufacture of synthetic antimalarials in India and have achieved a certain amount of success but then again one should remember that there are limitations in this field also, as India has to depend on others for quite a large number of basic chemicals which are imported from foreign countries.. Attempts have, therefore, been made to search for a satisfactory substitute when there are possibilities of the quinine supplies being inadequate to meet the demands of the physician. Experiments were, therefore, conducted in order to get over the difficulty of procuring the requisite quantity of quinine for each case.

Search for an Indigenous Remedy

The possibility of obtaining some indigenous herb which could either replace quinine or even supplement it to a certain extent as an antimalarial remedy was always thought of. Our attention was first directed to *Alstonia scholaris*, popularly known as *chhatim* which enjoyed the reputation of having some antimalarial properties. People of Bengal and of many other parts of India had a great belief in *chhatim* as a febrifuge or antiperiodic and it is a common practice in the Ayurvedic treatment of medicine to prescribe this drug in the form of decoction (*pachan*) for malaria and other febrile conditions. After an extensive investigation with 'dita-bark' it was found that *chhatim* with quinine was as powerful an antimalarial drug as pure quinine itself and it was further observed that whereas a pound of quinine alone could serve only 70 persons (calculating on the basis of disbursement of 100 grains to each person) quinine when mixed with *chhatim* could treat about 200 patients. In this way the quinine requirement may be brought down to one-third of the total requirement of quinine. This preparation was named "ABN-61" and its efficacy as a specific antimalarial remedy was tried in cases of human malaria with great success. Control cases with quinine alone were also observed side by side to find out the amount of quinine required to bring about an effective cure. Although the minimum effective dose of quinine alone is 5 grains three times a day for 6 days, making a total of 90 grains, a greater amount is necessary in a large number of cases and still greater amount should be given to prevent relapses.

If the treatment of malaria is carried out with "ABN-61" the quinine requirement will be greatly reduced and individual cases will only require 12 to 18 grains to control the temperature and 36 to 42 grains of quinine to produce an effective cure. In quinine, the medical practitioners have found a genuine and specific remedy for the disease and have naturally pinned their faith so much as not to fall back upon any other drug when quinine can be procured. But we very well know that the present quinine stock will not be able to supply India's full requirements. From the report of cases (to be published in a later communication) it will be observed that the drug ABN-61 will go a very long way towards the solution of this problem.

Historical Note

The plant Astonia scholaris belongs to the natural order apocynaceæ. Its vernacular names, are Chhatim (Ben.), Saptaparna (Sans.), meaning seven leaf; Chhatim, Datyuni (Hindi).

Rheede (1678) noticed the medicinal use of the bark by the natives along with salt and pepper in febrile dyspepsia. Rumphius (1741) found that the bark was useful in catarrhal dyspepsia and in the febrile states consequent upon that affection and also for enlarged spleen. (Pharmacographia Indica, Vol. 2, 1891). Nimmo (1839) suggested the use of the bark as an antiperiodic. Gibson (1853) described it as antiperiodic.

In a report on the centennial exhibitions, presented to the American Pharmaceutical Associations (Transactions, 1877), it was stated that equal doses of ditain (obtained from dita-bark) and sulphate of quinine had the same medicinal effects while ditaine is free from any disagreeable secondary symptoms which were usual concomitants of large doses of quinine. The results arrived at with the alkaloid of dita-bark in Manila hospitals and also in private practice were simply marvellous. It was being employed with most satisfactory results in the Islands of Mindanao where malignant fevers were prevalent (quoted from Watt's 'A dictionary of economical products of India, Vol. 1,

1898). Cathcart (1879) in the *American Journal of Pharmacology* stated that 'the bitter bark of *Alstonia constricta* (the Australian species), sometimes called the native quinine, is in common use by the shepherds in the interior of Southern Australia as a domestic remedy for malarial fevers'.

Stille and Maisch (1896) reported that the dita-bark and its alkaloid was used successfully in intermittent fever in the East Indies.

The first report of Proceedings of Central Indigenous Drugs Committee of India (published, Calcutta 1901) showed that *A. scholaris* had some febrifuge effect which was not lasting. Stewart used it in one drachm doses and reported that in mild cases of fever it was as effective as quinine. Nailer (1901) used the drug in 14 cases of "ague" in Tanjore (Madras) and found that in all cases it caused the temperature to fall steadily in a short time; no persipration was induced but the urine was observed to be increased and high coloured (quoted from Kirtikar and Basu's Indian Medicinal Plants, 1911).

Goodson, Henry and Macfi (1930) studied the activities of *A. scholaris* and *A. constricta* on bird malaria and found that echitamine (alkaloid of *A. scholaris*) had only a feeble action in doses of 5 mgm.

Buttle (as reported by Sharp, 1934) showed the inactivity of alstonian sulphate in bird malaria.

Mukherji, Ghosh and Siddons (1942) used a 1 to 2 per cent solution of the sulphate of total alkaloids of *Alstonia scholaris* as an intramuscular injection in doses of 20 mgm. per kilo body weight in cases of induced malaria (*plasmodium knowlesi*) in monkeys. They observed that the drug failed either to retard or to control the progress of infection. Later, they prepared a tincture(1 in 10) from the powdered bark containing 1·3 grs. of total alkaloid per ounce. This was administered in doses of one ounce thrice daily in a number of cases of human malaria of which one was of *pl. vivax* infection and three of *pl. falciparum* infections. They found that the drug had no demonstrable antimalarial action as it did not produce any remarkable febrifugal effect or alter in any significant way the course of infection.

From the above it will be found that the drug was found to be highly satisfactory by earlier workers while subsequent observations mostly applied on bird malaria and monkey malaria tend to prove the inefficacy of the drug in malaria infections. Such were the conflicting reports on the antimalarial property of *Alstonia scholaris.*

Present Observations with Aisotonia Scholaris

A series of preparations were made from dita-bark alone which were used in cases of human malaria. In the earlier works a very satisfactory result was not obtained as hoped for. In some cases, however, a beneficial effect by the administration of pure *chhatim* (dita-bark) was observed in that it either delayed the onset of the next paroxysm or reduced the duration of the next paroxysm. Daily examination of the blood showed that in earlier phases of infection the drug lowered the parasite count but could not retard the progress of infection. Later, a preparation was made in the form of tablet with *chhatim* (dita-bark) and quinine which was named 'ABN-61". This latter drug was then experimented on a series of cases of human malaria and found to be very effective. Case no. 1 shows that 14 tablets of AB-7 (preparation of dita-bark only) could not control the temperature while 10 tablets of ABN-61 (preparation of dita-bark and quinine) had a definite effect on the temperature and parasite count.

"ABN-61" as an Antimalarial Remedy—The therapeutic action of any antimalarial drug is usually first tested on either bird malaria or monkey malaria and then finally applied on human malria. It is quite resonable that before a drug is applied on human cases, a preliminary biological test on animals is necessary to select only those drugs which give indications for further study. The present observation was, however, directed mainly

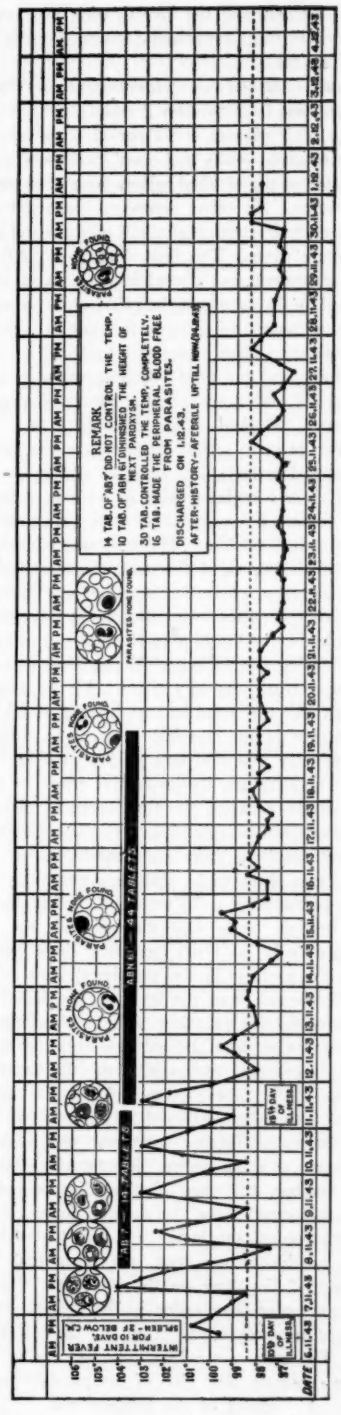
REMARK
14 TAB. OF AB7 DID NOT CONTROL THE TEMP.
10 TAB. OF ABN 61 DIMINISHED THE HEIGHT OF PARASITAEMIA.
30 TAB. CONTROLLED THE TEMP. COMPLETELY.
16 TAB. MADE THE PERIPHERAL BLOOD FREE FROM PARASITES.
DISCHARGED ON 1.12.43.
AFTER-HISTORY-AFEBRILE UPTILL
AB7 — 14 TABLETS
ABN61 — 30 TABLETS
PARASITES NOT FOUND
INTERMITTENT FEVER FOR 10 DAYS.
SPLEEN - 3F BELOW C.M.
DATE

Chart of a case of benign tertian malaria (case no. 1) showing quotidian type of temperature. Two generations of *plasmodium vivax* multiplying on alternate days. Circular diagrams on the top show the forms of parasites as found in the peripheral blood examined by thin film method. AB 7—Tablets of *Chhatim* only. ABN-61—Tablets of *Chhatim* and Quinine.

against human malaria and the investigation was conducted on patients admitted in the Carmichael Medical College Hospitals, Belegachia (Calcutta).

Dosage and Method of Administration—The general method followed was to administer 2 tablets of "ABN-61" three times a day to adult persons for a period of at least six days. The tablets were given orally and were swallowed with the aid of drinking water or the crushed tablets were dissolved in water before being taken. No other accessory treatment was introduced except the administration of alkali mixture and intravenous glucose in certain cases. The final dosage of "ABN-61" and the course of treatment was altered in some cases which were, however, guided by the nature of the effect observed on temperature and parasite count. In children the dose of "ABN-61" was modified accordingly. Each tablet of "ABN-61" contained only 1 grain of quinine and the total requirement to cure an attack was about 36 to 42 grains given in the course of 6 to 7 days.

Experimental Method—The methods of observation followed in the present series were to confirm all cases of clinically diagnosed malaria, *i.e.*, cases of sudden onset of fever with chill and rigor associated with or without enlargement of the spleen, by finding the malarial parasite from a microscopical examination of thin blood film. The drug was administered only in those cases which revealed the presence of malaria parasite. Further in every case where the parasite was detected in the peripheral blood, the patient was allowed to have the malarial paroxysm while in the hospital and then the treatment was commenced. During the period while the drug was withheld a simple alkaline mixture was only given. All the cases in which the drug "ABN-61" was tried had no history of taking quinine prior to admission in the hospital. After the drug was administered particular attention was paid regarding its effect in controlling the temperature, its destructive effect on asexual and sexual forms of the parasite, the time taken to make the peripheral blood from parasites, its effect on enlarged spleen and any untoward effect resulting from its administration. The parasiticidal action was observed by making a parasite count before the drug was commenced and then daily during the course of treatment. After the drug was discontinued, the blood was examined occasionally to check whether there was any reappearance of the parasite in the peripheral blood. Before the patient was discharged from the hospital, the blood was again thoroughly examined for parasites both by thin and thick film methods. Those cases who showed crescents (gametocytes of *pl. falciparum*) were not discharged from the hospital till the crescents disappeared. These forms of parasite are resistant even to quinine but can be destroyed by plasmochin. But in the present observation no further treatment was given and the crescents showed a spontaneous degeneration and gradual decrease in number till they finally disappeared. As the gametocytes are formed from the asexual forms, it is evident that the destruction of the latter will eventually lead to the disappearance of the former from the peripheral blood. To study the effect of the drug on the incidence of relapse, the patient was kept under observation in the hospital for a period of one fortnight to three weeks from the time of cessation of temperature. The cases were then followed up by instructing the patient to intimate any rise of temperature and further to submit a weekly report of the temperature.

Summary of the Results of Observation—The criterion of cure in malaria with any specific antimalarials is judged from its effect in controlling the temperature, causing the disappearance of the parasite from the peripheral blood and preventing the occurrence of relapses or lowering the incidence of relapse rate. Results obtained by treating cases of human malaria with the drug "ABN-61" so far fulfils all the above criteria. The present investigation on human malaria showed that 12 to 18 tablets of "ABN-61" administered in the course of 2 to 3 days were required to control the temperature and another 6 to 12 tablets were necessary to make the peripheral blood free from parasites. Excepting the gametocytes of *plasmodium falciparum*, the drug was found to have a powerful destructive effect on all species of malarial parasites which infect man. The drug had a definite inhibitory effect on the schizogony cycle. Daily examination of the blood during treatment showed a striking reduction in the number of parasites. In some cases a clear evidence of degeneration of parasites was obtained. The drug, therefore, exerted some physical effects of varying degrees and altered the morphological appearance of the parasite.

Conclusion

The present study justifies the recommendation of "ABN-61" as a safe antimalarial remedy as it was found to have marked parasiticidal action on all species of malarial parasites with the exception of the gametocytes of *plasmodium falciparum*. Further, while under the treatment of "ABN-61" the patient did not complain of any disagreeable symptoms (tinnitus and deafness) as are associated with cases treated with effective therapeutic doses of quinine (varying from 45 to 90 grains or more). This is, therefore, a distinct advantage over quinine. In the present series of cases no idiosyncrasy to the drug has yet been observed.

Acknowledgment

Our thanks are due to Messrs. Gluconate Ltd. who have helped us considerably in carrying out this investigation. The tablets ABN-61 and other tablets of *chhatim* only and also of *chhatim* and quinine as required for the present investigation were prepared by the same firm and were supplied to us free of cost.

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UNCONFIRMED REMITTENT FEVER IN LUCKNOW

H. SAHAI, M.B.B.S., RAI BAHADUR,
Professor of Medicine, King George Medical College, Lucknow
AND
N. GUPTA,
Lecturer of Pathology, King George Medical College, Lucknow

Introduction

During the summer and rainy season 1942, a peculiar set of cases of remittent fever were treated in our hospital, out of which 8 were fully investigated. The total number of such cases in the outdoor and indoor was about 30.

All these cases of continuous fever resembled very much cases of typhoid fever but with certain marked differences to be described later. *All* of them were characterised by 2-8 weeks of remittent fever, splenic enlargement as early as third or fourth day; absence of toxæmic symptoms and absence of common complications of enteric group of fevers. These cases started coming in about the second week of August in rapid succession and stopped after about the last week of September. Most of the patients who came to our hospital were adult males.

Symptoms and Signs

Premonitory Symptoms—The patients described a feverish feeling in the afternoon or in some cases early in the morning which went on for a day or two repeating itself at the same time, but this did not stop them from their daily work. Two patients complained of slight headache and giddiness for two days preceding the fever. On the onset of fever constipation was complained of as a rule and insomnia was present in some cases. There was slight malaise but no aches and pains in the body were complained of.

Onset—This feverish feeling gave rise to higher temperature in two to three days' time. The onset was marked with a definite chilly feeling or even shivering and temperature found to have risen up as high as 102°-103°F in the cases in which it was recorded. In four cases there was complete absence of initial feeling of cold. It was the rise of temperature which made them suspend their work.

The temperature was remittent in type and continued for 2-8 weeks, usually ranging from 100°-103°F. morning and evening respectively. The highest recorded temperature in these cases was 105·8°F. This persisted for 1-2 weeks usually. In one case it lasted 5 weeks.

Towards the end it tended to be more of hectic nature coming down to normal in the morning and rising to 102°-103°F. in the evening. The fall of temperature was mostly by lysis, the daily range getting lower and lower and settling down in about another week's time. The feeling of chill lasted only 3-4 days preceding the rise of temperature in the afternoon.

The spleen was found enlarged from 1½ to 3 fingers, below the costal margin, firm to touch as early as the 4th day of fever. The early rapid enlargement was evident from the history of pain and tenderness in the splenic region, the history of which most of these cases voluntarily offered.

The appearance of the cases was absolutely non-toxic and did not present the dull and apathetic picture so typically seen in typhoid fever.

The tongue was moist and became only slightly coated when the temperature reached its highest level.

Bowels were usually constipated and glycerine enema had to be resorted to on alternate days which gave satisfactory results.

The pulse was slow corresponding to the temperature but not so slow as that found in the enteric group.

Emaciation and exhaustion, though present, were never so marked as one finds in cases of the enteric group. These patients were cheerful all along and never showed "typhoid facies" even though high temperature continued for over 8 weeks.

Pathological Findings

(1) Blood picture showed, in the majority of cases, leucocytosis varying from 9 to 16,000/c.mm., during the whole course of the disease. A small number of cases, however, had a count of 6-8,000/c.mm. The polymorphs did not show any marked increase ranging from 68-75 per cent.

(2) Repeated blood cultures in these cases from 4th to 40th day were always sterile.

(3) Widal test against T.A.B. including 'O' & 'Vi' antigens was completely negative in all of them done repeatedly throughout the course of the disease.

(4) Stool culture done in 5 cases during 2nd to 4th weeks showed absence of non-lactose fermenters and streptococci.

(5) Urine culture done in 7 cases during 2nd to 4th weeks was sterile.

(6) Lumbar puncture done in one case did not reveal anything abnormal in physical, chemical, microscopical and cultural tests.

(7) Agglutination reactions were carried out with the bacterial emulsion from the stool culture of three of these cases with their own sera and with that of a confirmed case of typhoid from the wards. The tests were negative completely. Cross-agglutination tests were next tried with the bacterial emulsion from the stool culture of this typhoid case against the sera of the three cases but they too were negative.

(8) Blood films were carefully examined for malarial parasite but all were negative.

(9) Animal experiments: (*a*) A guinea-pig was injected intraperitoneally with 5 c.c. of blood on the 5th day of fever of one of these cases within 15-30 seconds of withdrawal from the patients' vein. Another 5 c.c. of blood from the vein of a healthy individual were injected in the same way into another guinea-pig used as a control. The temperature was recorded every 6 hours, there was an initial sharp rise in both, settling down to normal by the second day and then showing no abnormality.

(*b*) A teaspoonful of stool of a case during 4th week was given mixed up with its food to a guinea-pig and its temperature recorded morning and evening for 2 weeks but no change was found.

Complications

Mild bronchitic signs were noticed in two cases during the 3rd and 4th week and one case showed blood in stools but the recovery in all these was uneventful.

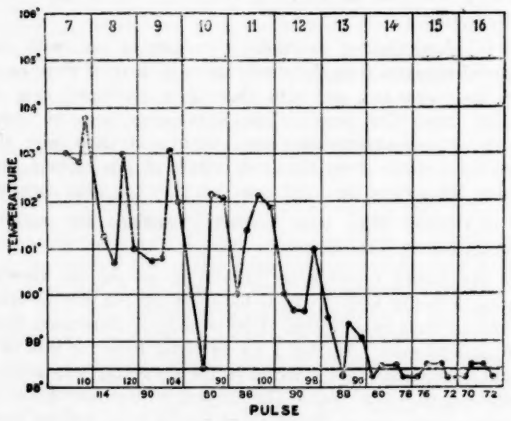
Comments

These cases in their course resembled cases of enteric group but the chief points which did not confirm the diagnosis of enteric fever were:—

(*i*) Non-toxic, cheerful appearance of the patients. (*ii*) Tongue moist and slightly coated, if at all. (*iii*) Enlargement of the spleen early and to a greater size than one expects in enteric group of fevers. (*iv*) Leucocytosis in the majority of them during the whole course of the disease. (*v*) Absence of abdominal symptoms. (*vi*) Repeated blood cultures and Widal tests completely negative throughout. (7) Uneventful course without complications and mortality.

Illustrative Cases

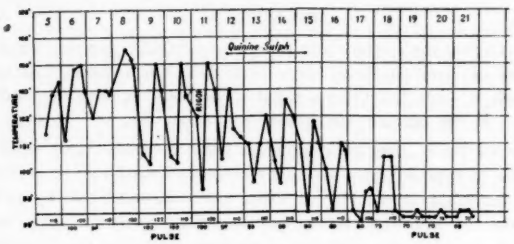
Case No. 1—R. C. aged 26 years, motor driver, admitted with complaints of fever for 7 days with headache and pain in abdomen. There was history of exposure in rain 8 days back which was followed by chilliness and feverish feeling the same evening. He felt better next morning but the chill and fever repeated themselves next day, since then he was confined to bed. His general appearance was quite cheerful and absolutely non-toxic, had a clean moist tongue. His spleen was firm and enlarged 1½ fingers below the left costal margin. No other physical signs could be detected anywhere. Investigations showed (*i*) Total W.B.C. count—8,500/c.mm. with polymorphs, 69% and lymphocytes, 31%. (*ii*) No malarial parasites could be detected in the blood film. (*iii*) Widal test against T.A.B. including 'O' & Vi.' antigens completely negative on 10th day and 15th day. (*iv*) Blood culture done on 7th day was sterile.



Case No. 1

Quinine was tried in 10 grain doses thrice daily for 6 days but without any effect. He had another rigor on 9th day of illness followed by 103°·2 F temperature. Temperature settled down on 14th day after an uneventful course.

Case No. 2—C. S. adult male, was admitted with complaints of fever and pain in the body for 5 days. The history of onset was with a rigor in the afternoon followed by fever in the evening. The rigor and fever were repeated next day as well. Physical signs revealed spleen 3 fingers enlarged and firm to touch. His tongue was clean and moist. Lungs and heart were normal.

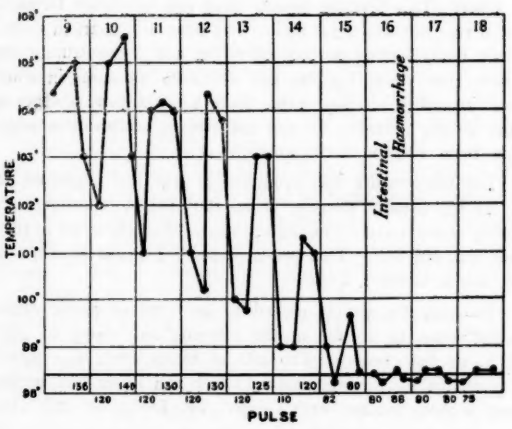


Case No. 2

Investigations showed—(*i*) Total W.B.C. count—16,400/c.mm. with polymorphs 60%, lymphocytes 39% and large mono 1%. (*ii*) Widal tests on 11th, 19th and 20th days completely negative against T.A.B. and 'O' and 'Vi' antigens. (*iii*) Urine culture on 15th day sterile. (*iv*) Stool culture on 20th day did not show anything of interest.

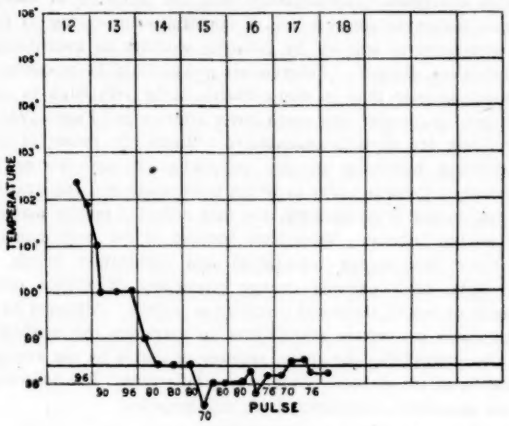
Progress—Glycerine enemata were given to relieve his constipation on alternate days. He had another rigor on 11th day of fever and then was put on quinine sulphate 10 grains twice daily for 4 days without effect. The illness lasted 20 days.

Case No. 3—B. aged 21 years, male barber was admitted on 9th day of fever with constipation. There was a history of chill at the onset. His spleen was 2 fingers enlarged below the costal margin.



Case No. 3

Investigations showed (*i*) Total W.B.C. count—16,800/c.mm. (9th day) with polymorphs 78% and lymphos 22%. (*ii*) Widal test against T.A.B. completely negative on 11th day and again on 17th day. (*iii*) No malarial parasites could be detected in the blood film. (*iv*) Blood culture on 9th day and 14th day were sterile. He passed slight blood in stool on 16th day.



CASE NO. 4

Case No. 4—K.N.T. male aged 17 years, student, admitted with complaints of (*i*) Fever for 12 days, (*ii*) Cough—6 days. (*iii*) Headache occasionally. (*iv*) Pain in abdomen—in splenic region.

History—He felt headache and giddiness for 3 days before fever and was constipated for 2 days. He kept on attending school till he felt feverish and he recorded 103°F in the evening. There was no chill or rigor. Insomnia was complained of. He took some quinine before coming to the Hospital.

Physical signs showed a cheerful disposition without any toxæmia. Tongue was slightly coated but moist. Spleen was 2 fingers enlarged *firm and* tender. The patient also complained of pain in splenic region.

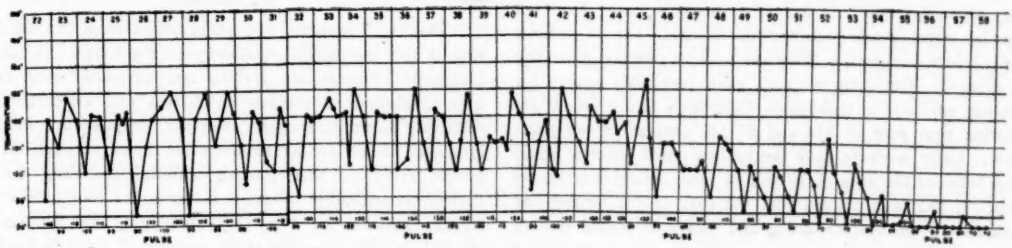
Progress—Temperature came down on 14th day but he was cheerful throughout and asked for food.

Investigations showed (*i*) Total W.B.C.—8.960/c.mm. polymorphs 12%, lymphos, 88%. (*ii*) Blood culture—sterile on 13th day. (*iii*) W.R.—completely negative. (*iv*) Sheep corpuscle hæmolysis test completely negative.

Case No. 5—L.U. male, aged 20 years, servant by profession, admitted with complaints of fever and slight cough for 20 days. There was history of shivering before rise of temperature for 3-4 days daily, the temperature being of hectic type. His bowels had been regular.

Physical signs showed: Bright eyes with moist slightly coated tongue, throat was slightly congested. Pulse was on slower side. Spleen was 2½ fingers enlarged and hard (there was no past history of a malarial attack). A few bronchitic signs were present in the lungs.

Investigations showed (*i*) Total W.B.C. count—6,400/c.mm. with polymorphs 56%, lymphos 44%. (*ii*) No malarial parasites were detected on blood film examination. (*iii*) Blood culture was sterile on 25th, 47th and 56th days of illness. (*iv*) Sputum was negative for T.B. (*v*) Widal against T.A.B.



CASE NO. 5

on 22nd and 32nd days completely negative. (*vi*) Urine culture —sterile (4th week). (*vii*) Stool culture—negative for non-lactose fermenters (4th week).

Progress—Despite a 7-8 weeks course he was all through non-toxic and cheerful. He made an uneventful recovery without any abdominal symptoms.

NOTICE

Capt. K. L. Saha, M.B., has offered a gold medal for the best paper on any subject in Pharmacology to be read at the 1944 session of the All-India Medical Conference.

Research workers and investigators who intend to submit a record of their work on this subject, are requested to send six typed copies of their articles to the Hony. General Secretary, Indian Medical Association, 23, Hindusthan Buildings, Calcutta, so as to reach the latter by the 30th September, 1944.

16-12-1943.

P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

TUBERCULOSIS IN CHILDHOOD

P. K. GHOSH, M.B., D.T.M. (CAL.), M.R.C.P. (LOND.),
Physician, Chest Deptt., Carmichael Medical College Hospitals, Calcutta.

The problems of tuberculosis in childhood are many and varied. It will not be possible to take up all of them in this paper. The salient features of the problem will, however, be discussed; and an attempt will be made to give an approximate idea of:—

(*i*) the extent of tuberculosis in childhood, (*ii*) the disease in childhood and the points of difference between it and that in adult, both in type and prognosis, and (*iii*) the difference between childhood tuberculosis in this country, and that in Europe and America. Further, my observations here are mainly confined to the pulmonary forms of tuberculosis.

More and more cases of pulmonary tuberculosis in childhood are being recognised in India to-day than in the past. The reason is two-fold. Firstly, it has been a common belief among medical practitioners here that tuberculous disease of the lungs is a disease of the grown-ups. So the disease in childhood is not often recognised till it is well advanced. Secondly, India is not as much industrialised as the West. The resistance among its people is not so highly developed. Their children, therefore. lack the racial immunity, and fall an easy prey to tuberculosis.

The extent of infection in any community may be gauged by the *Mantoux test*. A Mantoux positive case does not necessarily mean active tuberculous disease, but in infants especially under one year, a Mantoux positive reaction generally means disease. The early workers gave very high figures for tuberculous infection in childhood—Calmette's figure was 9 per cent during first year of life and 87 per cent at fifteen years and over. Later workers gave the figures much lower at 45-55 per cent between the ages of 10 and 14 years, examining school children. It has been argued that the data of the former had been collected from hospital-going and therefore poorer classes, and those of the latter from school children who consisted of a mixed class of people. But even then comparison at the same clinic early this century and in recent years definitely shows that tuberculosis infection in childhood has decreased. Hamburger's (1909) figure for tuberculous infection in Vienna in 1909 in children 15 years and over was 94 per cent. Under almost similar conditions, Dietrich (1937) one of Hamburger's own pupils, reported that less than half of the children at the same age were found to be infected on examination. This definitely shows that better preventive measures are now prevailing in Europe than in the past. Again, rural children are less infected than urban children. The infectivity in this country given by Ukil (1921) on testing 6500 persons of all ages was 11·8 per cent under 5 years and 35·3 per cent under 15 years. A recent investigation carried out under the auspices of the Bengal Tuberculosis Association (Annual Report, 1940) in an Orphanage in Calcutta for all children was 80 per cent (211 out of 261 positive to Mantoux test). These last two figures, however, indicate that the conditions in India as regards infectivity have not improved during the last decade, but may probably have worsened.

The importance of *contact* is well seen. Thus the percentage of infection among home contacts is much more than among non-contacts, and that the younger the child the more marked is this difference. Investigations into the incidence of tuberculous disease in contacts are of doubtful value owing to the different criteria adopted by different workers as constituting "tuberculous disease". Tuberculosis mortality in home-contacts is much greater than in non-contacts, being very high in the first year of life and very much lower afterwards (Pagel, 1942).

There are no data available to estimate the extent of the tuberculous morbidity in any population to any degree of reliability. Even in cities in which notification and registration of this disease is compulsory, the data collected in this manner are almost invariably incomplete because of the large number of cases that escape notification and duplication which is inevitable when patients change physicians or clinics often enough to render statistical compilation useless. Attempts have been made by certain statisticians to ascertain the morbidity rate by multiplying the annual number of deaths by the average duration of the disease. This is also fallacious. The following is an imperfect compilation from my hospital.

No. of Tuberculosis Cases

All Cases		*All ages*	*Child*
Chest (Out patients) ..	2790	1201	65 (5·4%)
Child (In patients) ..	297	—	14 (4·7%)

Pathology

The child presents two peculiarities from the adult. The first is the *anatomical peculiarity* in the lungs. In adults the lymphatic channels are scarred and narrowed as a result of dust inhalation or disease—in infants and children they are relatively large and open. Further, only scanty amounts of lymphoid tissue act as dampers or filters through which the lymph flows so that foreign material including bacilli are carried more readily to lymph nodes at the root (Miller, 1937). "This explains the relatively free lung and enlarged hilar shadow in this age—this facile passage of tubercle bacilli from lung parenchyma also explains frequent absence of caseating focus in lung, although exudative (allergic) focus is not so rare."

The second is the *immunoallergic* factor. Immunity is inherited to a certain degree but the greater immunity develops after infection has taken place. The infant or child gets the primary infection, if the dose is heavy, he or she may have a rapid primary focus followed by general dissemination and death. Often the primary infection, if trivial, causes no symptoms beyond a few day's fever and malaise with full recovery. The individual now enters into the second phase of allergy or hypersensitiveness. Allergy fluctuates, it is high early after infection and tends to diminish when infection has long been established *i.e.*, it is high in childhood and low in adults. Hence in childhood the reactions both clinical, and radiological in lung parenchyma may be high but they tend to subside and the individual gets well. Closely bound up with

allergy is immunity. The two are different, but both arise as a result of infection with the tubercle bacillus. Some writers go so far as to say that allergy is a measure of immunity, while others hold that the two are different. Some regard the limitation of tubrculous process to one organ, as is found in the isolated pulmonary tuberculosis of the adult as a sign of immunity, which has been developed by the individual as a result of previous infection. This immunity is as a rule not fully established in childhood. In childhood one, therefore, comes across more cases of disseminated tuberculosis including miliary tuberculosis, and the *childhood type of tuberculosis* of lung, *viz.*, parenchymal involvement of the lung, more or less or even subminimal, with corresponding draining lymph glands in the tracheobronchial group largely involved, the last with subminimal lesion in lung, constituting the *hilar tuberculosis* of early days.

Another point to which attention is being generally drawn is that the bone tuberculosis or genital tuberculosis should not be regarded as a primary disease, but that they all occur after primary infection, and result from the temporary bacillæmia which follows the primary or first infection.

Clinical Types

Griffith and Mitchell (1937) have given the following classification in their book on diseases of infants and children:—

Primary Tuberculosis—(Childhood type) (1) *Ghon's focus*—Calcified lesion in upper or lower lobe—it is usually single. (2) *Diffuse Infiltrative lesions* or bronchopneumonic—they pass as bronchopneumonia, the clinical findings in the lungs are the same but the course is longer. (3) *Hilar Tuberculosis*—the lung parenchymal lesion is subminimal and is often not visible in the x-ray, the glands at the root are enlarged. Many physicians, however, doubt whether hilar tuberculosis can be regarded as a clinical entity of pulmonary tuberculosis. (4) *Epituberculosis* (Eliasberg and Neuland)—A diffuse broad shadow, broader at the periphery and narrower towards the hilum is seen in certain cases. This shadow clears up in the course of 8 to 12 weeks. It is regarded as either of the three conditions: (*a*) perifocal inflammatory œdema, as a result of hypersensitivity in the child, (*b*) atelectasis, the result of pressure on bronchus supplying the parenchyma by enlarged tubercular gland, or the result of caseating bronchitis emerging from the primary focus, (*c*) the result of tuberculous pneumonia without tendency to caseation and, therefore, favourable for complete resorption (this form can be reproduced by intratracheal injection of dead or virulent bacilli in allergic animals (Pagel, 1942). (5) *Generalised or Disseminated form*—When there is a hæmatogenous spread, and several organs are involved simultaneously.

Adult or Reinfection Type—(1) Tuberculous pneumonia. (2) Phthisis—Caseating type, less involvement of larynx and intestines, base in child more often involved than in adults. (3) Acute miliary tuberculosis.

In this connection the main points of difference between 'childhood' and 'adult' type of tuberculosis may be enumerated. In the *childhood type* the lesion in the lung is the result of a primary infection and may occur in any part, and is usually associated with enlargement of the corresponding tracheobronchial lymph glands. The lesion commonly resolves leaving little or no scar, except when caseation has occurred which usually becomes calcified. Prognosis is generally good. The *adult type* usually occurs in adults but may also be found in children. The lesion in the lung is the result of a reinfection and is usually localized in the upper part but the corresponding tracheobronchial glands are not enlarged. The lesion ulcerates and may be followed by excavation or fibrosis or by both. Prognosis in children is generally bad.

Symptoms and Signs

Cough, wasting, fever, rapid pulse, hæmoptysis, one or all may be present. In adults, cough, fever and wasting are present in this sequence whereas in children, the sequence is reversed. While *cough* is the prime symptom in adult tuberculosis of lungs, it is surprisingly not so in chilldren. The most important thing in the children's history is wasting and getting off colour or not thriving well. *Fever* is usually present, but it may be noticed after wasting, either it is a later phenomenon, or else is a less presenting symptom. It may be absent even when parenchymal lesion is extensive. The fever in miliary tuberculosis is typhoid in type, but it may be high or low intermittent or of irregular form. In this connection, it must be remembered that the temperature of many normal children may be 100·0°F.; variation of 1·5°F. in the twentyfour hours has some significance. *Rapid pulse* is usually associated with tuberculous disease. But it is a less reliable guide in early life, as the pulse in this period is usually higher; and the least psychic or other disturbances may cause a sharp rise in the pulse rate. *Loss of appetite* and *listlessness* are other signs. *Hæmoptysis* is less commonly seen in children compared to adults, and many such cases are non-tuberculous. But hæmoptysis should always arouse suspicion and must be fully investigated. *Dyspnœa*, as a result of spontaneous pneumothorax has ben noticed as the first symptom in several cases. It may also occur as a result of pressure on trachea and bronchi by enlarged tracheobronchial glands. *Pleurisy* with effusion heralding tuberculosis is much less common in childhood. But there may be a complete absence of all symptoms and the case may yet be one of tuberculosis. This happens specially when the child is very young and has not learnt to express itself.

Signs are not different from those found in adults. But persistent râles which are stressed in adults as sure signs of tuberculosis, may often lead to a mistaken diagnosis in childhood.

Prognosis

Prognosis varies with age and clinical type of the disease.

The first infection in infancy or in childhood may arouse no suspicion or, it may raise a storm. Generally speaking within the age of one year, the mortality rate is high. It may be the result of low resistance of the individual or of a bigger dose due to intimate contact, or of a combination of both factors. Thereafter the mortality rate is low till 14 years. *Healed primary* lesion means that the child has not only 'acquired' resistance as a result of infection, but has also high "natural" or "inherited" resistance as shown by his overcoming the primary infection. In the *childhood type of* tuberculosis and in epituberculosis, the prognosis is generally good. After a short or protracted course the child recovers. In the dissemi-

nated form, however, the prognosis is bad, death in many cases result from terminal tubercular meningitis but recovery may take place quite unexpectedly in rare cases. Persistent *enlargement of spleen* is bad prognostically, as it is present not infrequently in disseminated forms but its significance in India is less, due to the associated tropical diseases. In *acute miliary tuberculosis*, death occurs within 3 months. In *chronic miliary tuberculosis* Hoyle and Vaizey (1937) noticed that the longest period an individual could live was ten years but the time of survival is usually less, death occurring within 6 months to 2 years. In *adult* type of lung tuberculosis in childhood, the prognosis is usually grave, and probably worse than in adults. The cases with cavity fare worse than those that are without it and cases with multiple cavities fare still worse.

Diagnosis

When fever is prominent, tuberculous disease in childhood should be differentiated from malaria, typhoid fever and B. coli infection. When lung symptoms predominate, it should be differentiated from infections of upper respiratory passages, bronchiectasis and pulmonary abscess. A careful history, especially with regard to history of contact, even in presence of conflicting symptoms, often clinches the diagnosis. A tuberculin test, examination of the sputum and of gastric contents, and a radiological examination of the chest will settle the diagnosis in the great majority of cases.

Tuberculin test—A positive tuberculin test under one year may be taken as indicative of tuberculous disease but thereafter it means infection and not disease. *Mantoux Test* done with intradermal injection of Koch's old tuberculin or better still with its purified protein derivatives called P.P.D. (first injection of 0·00002 mgm. if negative, inject 0·005 mgm.) is universally employed. A *Patch Test* done with paper soaked in 0·001 mgm. old tuberculin and sticking it with adhesive plaster on the skin, is being extensively used in America in recent times. It is claimed to be as efficacious, and has the advantage of not frightening the children as no injection is involved.

Examination of sputum and gastric contents. Children usually swallow sputum and cannot bring it up. Still an attempt should be made to obtain some. If successful, the sputum can be examined for tubercle bacilli. If this smear is negative, a concentration method (antiformin method) may be employed and the bacilli searched for. If the child cannot bring up sputum, and if he is not old enough, he can be induced to cough on the laryngoscopic mirror held over the epiglottis with the mouth open. If sputum cannot be obtained by any of these methods, the empty stomach after the night's rest and before breakfast, is lavaged with normal saline by means of a Ryle's tube, and the contents withdrawn, centrifuged and searched for tubercle bacilli. Stool examination is tiring, but occasionally gives positive findings on smear examination by concentration method, or on animal inoculation.

Radiological Examination—It is the surest method as yet for detecting tuberculous disease. Of course, x-ray examination has its fallacies, but with modern improved techniques (specially tomography) the failures to detect the disease have been very much reduced. Certain types of lesion throw little or no shadow on the film; while others which contain calcium produce heavy ones. Small caseated foci are only slightly radio-opaque. Tracheobronchial lymph-nodes, unless calcified or greatly enlarged, may not throw a good shadow. But it should be borne in mind that calcified foci do not necessarily mean inactivity in the lesions. Serial films taken at intervals of three months or more, depending on the conditions of the case, prove sometimes of great value in prognosis as well as in diagnosis. While it must be admitted that there is no appearance in a chest film which is pathognomonic of tuberculosis, yet the interpretation of shadows in a chest film—their position, appearance, density, etc., by men experienced in the technique will lead to correct diagnosis of tuberculosis when other methods fail.

There are many other tests employed in the diagnosis of tuberculous disease. Some are fallacious, some are laborious and some have only an academic interest but none so sure as the above three methods.

Treatment

Prophylaxis—Calmette introduced his B.C.G. vaccine as a prophylaxis against tuberculosis. He originally gave it by mouth to infants on the 3rd, 5th and 7th days after birth. Later workers gave it parenterally in two doses of 0·01 mgm. and 0·1 mgm. at intervals of 2 weeks. A storm of controversy raged about its efficacy as a prophylactic measure and about its dangers, especially after the Lübeck disaster. But even barring Calmette, opinions in Scandinavia and in the United States confirm its prophylactic value, but this prophylactic value is very shortlived.

Curative—The curative measures are more or less the same as are employed in the treatment of adults. *Rest* is essential and should be absolute. Children do not take rest so easily in the beginning. But once used to it, they will not resist. Rest is best attained in sanatoria, where they see others resting and, therefore, easily imitate them. When they are cured and discharged from sanatoria, they should carry on with their studies, but under medical supervision. For them preventoria and open air schools have been started in the United States. *Dietetics* is more important in children than in adults. Children require more calories per pound of their body weight to maintain growth. Again, there is loss of weight due to the disease. So the children are allowed an abundance of diet. The growth promothing vitamins must be amply provided for; fat-soluble vitamins A and D, and the water-soluble vitamin C are necessary. The daily diet must, therefore, contain a liberal supply of milk, butter, fruits, cereals, and sufficient protein in the form of eggs, fish and sometimes meat. Calcium is much needed for the growing bones. The calcium in the milk ought to be supplemented by calcium medication.

Medicines—Among a host of medicines employed in the treatment of pulmonary tuberculosis, there are only three worth mentioning, *viz.*, calcium, gold and tuberculin. *Calcium* has no specific value in tuberculosis. But in exudative lesions, and in cases of slight hæmoptysis it can be used with benefit. Calcium may be given parenterally, either intravenously as calcium chloride or intramuscularly as calcium gluconate. But small children are afraid of injections. Various salts are prescribed by mouth. The lactate and the gluconate are the only palatable and absorbable drugs by this route. They are best given on an empty stomach, as the alkali tide after food

precipitates the calcium as phosphate. *Gold* is the other drug which has been extensively used in the treatment of tuberculosis. In acute exudative lesions with high temperature, gold should be avoided. When the temperature has been controlled, and the exudative phase is over and proliferative changes have begun, gold may be used. It is always given parenterally, either by intravenous or intramuscular route. In children veins are difficult to obtain, the child may be restless, and reaction may be high. Hence the intramuscular route is chosen. Gold is given in very small doses in quarter to half the dose of adults or less, according to age. It is given weekly for 12 weeks, and then an interval of 12 weeks should follow before gold is given again. In each course a total of 1·0 gm. or less is given. The preparations in common use in this country are sanocrysin, solganal-B and myocrisin. Solganal-B has been found to be least toxic. Though still extensively used the value of gold in the treatment of tuberculosis has been questioned. *Vitamins* are often given as supplementary medicines, but they have already been discussed under dietetics. *Tuberculin* is a specific remedy. It (tuberculin B.E.) has been used in adults in afebrile fibrotic cases. But its use in pulmonary tuberculosis in children is very much limited, and is better avoided altogether.

Artificial Pneumothorax—Artificial pneumothorax has not been extensively used in children. But there is no contra-indication to its use. It has been employed even in infants under one year. The largest series of artificial pneumothorax cases in childhood has been reported by Voltchok (1937). In his series of 82 cases, 27 were under one year. In 63 treatment was completed, the results on the whole were not very satisfactory. Thus 25 cases with multiple cavities with dissemination derived no benefit; in 27 unilateral cases with cavity 10 were arrested, 3 improved and 14 were worse; in 11 unilateral cases with no cavity and with sputum negative 3 were arrested, 4 improved and 4 were worse. Duration of collapse was 4 months on an average and 11 months the maximum period. The most frequent complication was subcutaneous emphysema which occurred in 38 out of 82 cases (43 per cent).

Surgical Methods—Surgical operations on the chest are not contra-indicated in children. But as children grow up, deformities may result. Thoracoplasty has been followed by marked scoliosis in many.

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MEDICAL PREPAREDNESS SERIES

THE MODERN TREATMENT AND PREVENTION OF VENEREAL DISEASES*

V. GOVINDAN NAIR, M.R.C.P., F.R.F.P.S.,

Venereologist and Dermatologist, King George Hospital, Vizagapatam.

Venereal diseases number six. They are syphilis, gonorrhœa, chancroid, aphthous ulceration of the genitalia, granuloma venereum and lymphogranuloma inguinale. Leaving aside the fourth, aphthous ulceration of the genitalia, which need not be taken as a venereal disease, there are five well recognised venereal diseases. To discuss the treatment of all these in one paper is difficult. The object of this paper is not to discuss all aspects of treatment in every detail but to give in brief a general idea of the principles of treatment which may be useful to the general practitioner.

The treatment of venereal diseases may be prophylactic or curative. These diesases are preventable, particularly the big three, syphilis, gonorrhœa and chancroid. This has been convincingly proved during the last Great War. Prophylaxis is effective only if the measures are applied within the first three or four hours after the first exposure to infection. As regards syphilis, it is of value to a certin extent even up to the limit of eight hours alfter exposure. Moore's experience among the defence forces during the last World War was that prophylaxis failed to protect in only about 0·3 per cent of cases in which it was used. It was also his experience that prophylaxis was employed even by a controlled and disciplined group as the defence forces only if penalty was imposed. In civil life, generally speaking, no one ever thinks of prophylaxis, though provided for in some countries, out of ignorance, indifference and carelessness. So it would seem doubtful whether prophylaxis will ever become popular among the civilians, human nature being what it is.

The technique of prophylaxis in the male. Soon after exposure—the sooner the better—and not later than three hours after the first exposure, the individual should attend a prophylactic station if available where there is a trained attendant on duty. Such stations are provided in some countries. Needless to say, any medical practitioner will be able to attend to it. After passing urine he should expose himself from the umbilicus down to the middle of the thighs. This area should be thoroughly scrubbed and washed with soap and warm water, preferably green soap. The prepuce should be retracted and the penis including glans, balanoprepucial fold, frænum, penoscrotal angle, etc., should be thoroughly washed. This process should take five minutes. At this stage existence of any sores on the genitalia or discharge from the urethra should be noted.

Then inject one dram of a freshly prepared 2 per cent solution of protargol or 10 per cent solution of argyrol into the urethra. While the syringe is being removed the patient should be instructed to keep the meatus pressed by the thumb and forefinger so as to allow the solution to remain in the

* This is the eleventh of a series of articles on war medicine, A.R.P. and allied subjects which are being published since May, 1943.—Editor, *J. Indian M. A.*

urethra for five minutes. The prssure should be released once or twice to allow the solution to come in contact with the meatus. Then half to one dram of a 33 per cent calomel ointment made in equal parts of lanolin and lard is rubbed on to the penis taking care to reach all the folds and corners. Finally the genitalia are wrapped in oil paper and the patient sent to bed. He should not pass urine for three or four hours or as long as possible.

Thorough washing with soap and water is an adequate prophylactic for chancroid and partly for syphilis. The injection or instillation of solutions of silver salts in certain strengths serves as a good preventive for gonorrhœa and the rubbing of calomel ointment for syphilis as experimentally demonstrated by Metchnikoff.

1. Syphilis

Syphilis occurs as a disease only in man, but some animals like monkeys and rabbits can be experimentally infected. In the latter, infection disappears spontaneously by the agency of natural immunity. Syphilis is a ubiquitous disease. It is no respector of race, class, caste, creed or age. It is seen all over the world. There is not a single tissue in the human body which is not affected by sphilis, though it is essentially a disease of the vascular system. However, there are three structures in which primary syphilis is not encountered. They are the hair, the nail and the teeth.

Before considering the curative treatment of syphilis, it is essential to bear in mind a few facts about syphilis:

1. In approaching a patient of syphilis, rid yourself of the venereal conception of syphilis. Treat the question of infection as a matter of fact and very considerately. It is very difficult to convince the public that any one who is sexually clean may have a venereal disease; because by rigid definition, anything venereal has its origin in sexual wantonness. The term is not compatible with fact.

2. Syphilis is contracted in two ways, acquired and congenital or prenatal. In the acquired variety the infection spreads by the lymphatics of the skin or mucous membrane. In the other variety the occurrence of infection is intra-uterine.

3. The decade 1903-1913 is memorable in the history of syphilis. In 1903, Metchnikoff and Roux were able to produce syphilis in monkeys. In 1905, the causative organism of syphilis, *T. pallidum*, was discovered by Schaudinn and Hoffmann. In 1906, Wassermann, Neisser and Bruck applied the complement-fixation test in the diagnosis of syphilis which is now known as Wassermann test. In 1909, Ehrlich and Hata, as the result of laborious experimental investigations, produced a complicated organic arsenic compound for the treatment of syphilis and named it 606, the drug being the successful result of their 606th experiment. Ehrlich's objective was to produce a substance which would be a "therapia sterilans magnum' for syphilis. In 1911, it was marketed under the proprietary name of salvarsan.

4. Dividing the course of syphilis as primary, secondary, tertiary, quarternary, etc., is incorrect. These terms were introduced in olden days when it was considered that syphilis in the primary stage was a localised disease, that in its secondary stage it became generalised and so on. It has been definitely proved that syphilis is from the very beginning, even before it actually declares itself, a generalised systemic infectious disease. Neisser (1906-09) demonstrated that syphilis was a systemic infectious disease from the very commencement by recovering the organism from the bone marrow, spleen and testis within forty-eight hours after experimental inoculation and many days or even weeks before the appearance of chancre, the traditionally accepted initial or primary manifestation of syphilis. Kolle and Evers have shown that the spirochetes would reach the nearest lymphatic glands in rabbits in thirty minutes and in guinea-pigs in five minutes after inoculation. Though the results of these animal experiments cannot be totally accepted in the case of man there is yet reason to believe that syphilis in man ceases to be a local disease within two or three hours after inoculation. Thus it will be seen that syphilis would become a systemic infection long before its very existence has been suspected. Of late, syphilis has been rightly divided into early and late syphilis. In early syphilis the number of treponemata in the tissues and circulation is very large; they are free and thus easy of attack and destruction. In late syphilis the organisms are few and well protected by fibrous tissue and thus difficult to reach and destroy. This distinction is significant because the disease is far more communicable but also more readily curable in its early stage.

5. Categorise all genital ulcers either as syphilitic or non-syphilitic. This simple division is advantageous as a non-syphilitic ulcer is relatively unimportant, its effects being usually local, but a syphilitic ulcer is only the primary manifestation of a generalised infection which requires immediate treatment for eradication. If treatment is begun before blood tests prove positive, the cures are 33 per cent higher (Stokes, 1936) than those at any subsequent time. In the early stage a day less means extra treatment for weeks later and so much longer the patient remains a potential source of infection. Extragenital chancres may occur in any part of the cutaneous surface or the mucous membrane of the mouth. The common sites are the fingers, the lips and the breasts.

6. No antiseptics, even of the mildest type, should be applied to the sore till a definite diagnosis is made. Even the mildest antiseptic, soap and water or drying destroys the spirochetes.

7. Infection with T. pallidum can take place through any intact mucous membrane. Brown and Pearce have shown that even on the highly resistant vaginal mucosa of the rabbit no trauma is a prerequisite for the entry of the spirochetes. The break in the skin for the organisms to pass through need be only microscopic.

8. Though it is common to have a primary chancre developed at the site of inoculation, in some cases such primary reactions may be absent and the first evidence of syphilis may show itself in the adjacent lymphatic nodes instead of at the point of traumatic entry or only as the so-called secondary syphilis. This is often the case with needle prick infection—*syphilis d'emblee*. The question of a primary lesion does not arise in syphilis after blood transfusion.

9. The manifestations of syphilis are likely to be milder and less out-spoken in the woman than in the man.

10. Pregnancy and lactation play an important part in the woman's defence mechanism in syphilis.

11. Syphilis may be discovered in a woman at any time during her pregnancy and if she is given early and adequate treatment the offspring will have nine chances out of ten of being free from syphilis.

12. Infectiousness in syphilis can never be determined nor non-infectiousness proved by the result of serological tests, single or repeated. Syphilis is most infectious in its early stage and becomes less and less with lapse of time. It is rarely infectious after five years. Late congenital cases also are non-infectious.

13. Physical examination laying special emphasis on the inspection of the genitalia and lips is the chief procedure for determining infectiousness. Moist lesions only are infectious, the most dangerous to handle being the chancre, the moist papule (condylomata) and the mucous patch.

14. Syphilis is potentially communicable until it has been treated adequately for at least a year and for two or three years if treatment has been irregular or neglected. It is always potentially communicable during pregnancy to the progeny.

15. The treatment of late syphilis is essentially the detection of early and latent syphilis followed by prompt and thorough treatment.

16. It is in the treatment of late syphilis that the clinician must practise medicine as an art; for it requires great skill and sound judgment to strike the nice balance between the salvarsan, heavy metal, iodides and rest periods which will give the best result. Accurate estimation of the patient's general condition, of the effect of antisyphilitic treatment and of the effect of the latter on prognosis, may make all the difference between success and quick catastrophe.

17. Remember the maxim "always suspect syphilis, but be slow to diagnose it."

The treatment of syphilis has to be considered under two aspects; the treatment of early syphilis and that of late syphilis. In early syphilis the treponemes are present abundantly in the tissues and circulation and are free and, therefore, the aim of treatment is to attack these free treponemes and destroy them as rapidly and thoroughly as possible. The treatment should be continued till the infection is completely eradicated. Early syphilis includes primary and secondary syphilis of old nomenclature. According to Osmond (1942) it denotes syphilis in the first four years after the date of infection. The term late syphilis means syphilis of more than four years duration and includes tertiary and visceral syphilis, particularly neurosyphilis and cardiovascular syphilis. In late syphilis the treponemes in the body are few in number and hiding in the so-called backwaters of the viscera and well entrenched behind the barricade of fibrous tissue. The aim of treatment in this stage is to arrest further damage caused by the disease and to abolish the symptoms.

Before starting treatment the diagnosis must be made sure beyond dispute. In early syphilis this can be accomplished by the demonstration of T. pallidum in the serum of the chancre by the dark-ground illumination examination and/or by the positive serum tests, such as complement-fixation, the Wassermann, or precipitation, the Kahn test. A single positive test should not be accepted light-heartedly unless supported by clinical evidence or confirmed by a second positive result either in the same laboratory or in a different one. Certain diagnosis is all-important as syphilis is a very serious disease and its treatment is long, expensive and by no means devoid of risk. No person should be allowed to live under the shadow of doubt as to eventual cure without first removing all doubts as to the existence of the infection.

(*To be continued*)

CASE NOTE

SITUS INVERSUS VISCERUM WITH DEXTROCARDIA

K. P. BHATTACHARYA.
House Physician, P. W. Medical College Hospital, Patna.

Introduction

The term situs inversus viscerum designates an anomalous condition in which organs or viscera are transposed from their normal site to locations on the opposite side of the body. It may comprehend complete transposition of both the thoracic and abdominal organs or of only one or the other group, or a single organ of either group. Thus transposition of the heart from left to right is properly designated situs inversus cordis or dextrocardia. Frequently, the situs inversus is complete, that is, both abdominal and thoracic organs are transposed.

Cause—The exact cause of the transposition of organs in man is not properly known. Various explanations have been put forth:—

(*i*) Reversed lateralisation of early differentiating organs *viz.*, rotation of the stomach and heart loop. Ventral liver bud shifting to left from right.

(*ii*) Reversed spiral growth; clockwise pharynx to cæcum, anticlock anus to cæcum.

(*iii*) Pressler's toad embryo experiment.

(*iv*) Theoretically, the complete situs inversus viscerum might be the surviving member of an original pair of one egg twins or conceiveably even the right half of an original duplicate monster in which the left was resorbed.

Case Record

The case reported here is of clinical interest because it was diagnosed as a case of abdominal tumour but later on it proved to be a simple case of splenomegaly due to K. A. with spleen on the right side. Patient M. I., aged 40, fitter in Patna Electric Supply Company came to this hospital on 25-1-43 with following complaints: (1) Fever for 4 months, from Oct. '42. (2) Cough with moderate expectoration for 3 months, since Nov. '42. (3) Dyspnœa for 15 days only. (4) A swelling in the right half of the abdomen for 1½ months from Dec., '42; since last 15 days the swelling rapidly increased in size.

Past history—Occasionally fever, starting with a chill and lasting for a few days. Some years back he had double fracture of both the bones of the forearm.

Family history—He had two brothers, one died from respiratory disease. He has his wife and several children.

Personal habit—Teetotaller, but used to smoke before.

History of present complaints—Since last one year, he did not keep well. He took sick leave several times. He joined his work, as soon as he was afrebile or his leave expired. This went on till he was compelled by the company's Medical Officer to take leave for thorough treatment in this hospital.

On Examination: He was of low average build and in a low condition.

The positive findings were:—Heart apex beat visible and palpable in the right 5th intercostal space 1" inside the mid-clavicular line; it was forceful and localized over an area 1" in diameter.

Clubbing of the fingers of both the hands. Pulse regular, of fair volume and low tension. *In the chest,* signs of fibrosis and emphysema with marked catarrh in both the lungs were obtained.

In the abdomen, a huge solid mass, occupied the right iliac, right lumbar and right hypochondrium; the surface was smooth; the mass moved with respiration freely; anteriorly, a sharp margin could be felt and a notch near the middle of that margin was easily made out. Bimanually, with left hand behind in the renal angle and the other hand in front, the mass could be moved between the two hands.

The mass was dull on percussion; the dullness disappeared under the costal margin in front. Posteriorly, the dullness extended upwards along the 9th and 10th ribs, up to the level of the 8th intercostal space in posterior axillary line.

On auscultation, on the mass and abdomen, no bruit or signs of obstruction detected. The patient never complained of pain, frequency and/or hæmorrhage during micturition. Examination of blood showed leucocytosis with absolute and relative increase in the number of polymorphonuclear neutrophils and monocytes. Eosinophils and basophils were absent. Lymphocytes were within normal limits. In urine and stool nothing abnormal were detected. In sputum examination, no acid-fast bacilli were detected.

Provisional Diagnosis—Kala azar with enlarged spleen on right side due to situs inversus viscerum. Special x'ray screen examination with barium meal, electrocardiography, together with a strongly positive formol-gel reaction and the complete disappearance of the swelling with anti-kala-azar treatment confirmed the diagnosis of the case.

Differential diagnosis—The mass had to be distinguished from (1) An enlarged gall-bladder; (2) An enlarged Riedel's lobe of the liver, (3) Kidney tumours. (4) Tabes mesenterica.

Discussion

About frequency, the radiologists have found them to occur very rarely to the order of one in ten thousand cases. Here during the last ten years only three cases have occurred so far. Probably more might have been found, the condition being benign and symptomless never attract attention. One case was reported from Lansdowne Hospital, Udaipur, by Rai Bahadur Chhaggan Nath. Cases of pain in left side of the abdomen have (wrongly) undergone operations for acute abdomen when a left-sided appendix with situs inversus cæcum have been confirmed.

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P. B. MUKERJI,
Hony. General Secretary,
Indian Medical Association.

JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION
CALCUTTA, APRIL, 1944

LIQUID PARAFFIN

With civilisation man has become heir to many diseases of which probably syphilis and constipation are more known. No other animal except those that live with man, *e.g.*, cats and dogs is a victim to constipation. Constipation may be so distressing a condition that in severe cases the patients had been operated upon as they came wth the signs and symptoms of acute abdomen. So to relieve the condition by a habitual drug, which would not in any way interfere with the normal life of anybody has been the concern of both medical men and the suffering public, not to speak of the scrupulous and unscrupulous manufacturer of many aperients much advertised in the lay press. Of the few dozen of medicines, liquid paraffin was chosen to be a drug which could be safely recommended. It is fool-proof as there is no danger of over-dosage, no danger of toxicity as it is not absorbed from the intestine, motions are liquid and do not irritate any part of the gut, do not produce any after-effect and people become so pleased that they started to replace ordinary oils used in cooking and salads by liquid paraffin with the fond hope of killing two birds with the same stone. Incidentally, it was also cheaper than the ordinary vegetable oils. But the continuous bliss has not lasted long.

Dutcher and others[1] warned us in 1927 that continuous use of the mineral oil in food is the surest way of creating vitamin A deficiency, as liquid paraffin is a good solvent for carotene. Hence as the liquid paraffin leaves the intestine unchanged it takes all the carotene and, therefore, vitamin A along with it. This was further taken up by many other investigators and opinions became so very convincing that the Council on Foods and Nutrition of the American Medical Association took it up as a matter of investigation. Now they have submitted their reports[2] which confirm the earlier workers.

After careful consideration of all the points, very alarming conclusions have been derived. It has been found that the mineral oil can be sometimes absorbed with some carcinogenetic effect on various organs though a conclusive proof is not forthcoming. An ounce of mineral oil has been found capable of dissolving and carrying along with it 140,000 international units of vitamin A. The magnitude of the loss can be understood when we consider that an average American diet supplies from 5,000 to 10,000 international units of vitamin A. And our diet surely supplies less. The danger becomes manifold in the case of pregnant women and spare men who require but take less quantity of food and consequently suffer more from constipation. But the nefarious oil does not stop there; it interferes with the absorption of vitamins D and K, calcium and phosphorus and continual use of mineral oil will certainly produce rickets and other avitaminoses. Upamanyu[3] has recently reported three cases where the baneful effects of continuous use of mineral oil have been clearly demonstrated. Internists have also come forward to demonstrate that it is not only in the role of passive agent that it produces its deleterious effects but in some cases it has been responsible to produce lipoid pneumonia when used in ways other than to relieve constipation. The whole position has been well summarised by Eisenstaedt[4] who says, "It is generally held that the use of oily nasal drops, cod liver oil, liquid paraffin, etc., is injudicious in small or weak children as well as in debilitated conditions of adults and old age, summarily in all cases where difficulty in breathing and swallowing might provide the necessary mechanism for aspiration." To add to this, Morgan[5] has come forward to describe a syndrome,—"mineral oil poisoning",—which may be a concomitant of continual use of liquid paraffin. "The most frequent signs and symptoms are anorexia, indigestion, flatulence, fatigue nervousness, dyschezia and anal leakage, accompanied in many cases by considerable loss of weight."

Surgeons were not far behind and they came forward to opine that "Proctologists have experienced difficulty in visualising the wall of the rectum because of an adhering film of oil in persons who take liquid petroleum."[2]

Thus ends the reign of the most favourite and popular aperient. And the American Medical Association has withdrawn its acceptance of such products.[2]

REFUSAL OF ANDHRA MEDICAL GRADUATES FROM THE MEMBERSHIP EXAMINATION

We understand that the medical graduates of Andhra University have been refused permission to appear at the ensuing M.R.C.P. examination, now being held in India. The reason given for this is that Andhra medical degree has not yet been recognised by the General Medical Council of United Kingdom. Although the Indian Medical Council had recognised the Andhra medical graduates with retrospective effect in 1941 and recommended to the General Medical Council for reciprocal recognition, nothing happened during all these three years. Inspite of repeated reminders no news has been received regarding the final decision of the General Medical Council. It is the duty of the Indian Medical Council to see that the General Medical Council gives effect to its recommendations otherwise no reciprocity can exist between the two Councils. It is a matter which the medical profession should take up in right earnest and see that medical graduates of any Indian University are not discriminated in foreign countries.

To make the situation worse, the Indian Medical Council seems to have no control, or contact or say in the examination now being conducted in India by the Royal College of Physicians, London. It looks that any representation by the Indian Medical Council has to be made through the Government of India and Secretary of State to the Royal College of Physicians. Will the General Medical Council of United Kingdom allow the examining bodies say American or Indian to conduct similar examinations in the British Isles?

It is understood that the Indian Medical Council is probably proceeding on the usual lines to the Royal College. An attempt is also being made to approach the above body directly. We do not know what the matter is.

[1] DUTCHER, R. A., ELY, J. O., AND HONEYWELL, H. E.—*Proc. Soc. Exper. Biol. & Med.*, **24**:953 (June), 1927.
[2] *J. A. M. A.*, **123**: 967, 1943.
[3] UPAMANYU, L. K.—*Indian M. Gaz.*, **78**:442, 1943.
[4] EISENSTAEDT, K.—*Ibid*:619, 1943.
[5] MORGAN, J. W.—*J. A. M. A.*, **117**:1335, 1941.

CORRESPONDENCE

The Editor is not responsible for any views expressed by contributors.—EDITOR.

A PLEA FOR DELOADING AND REORGANISING PRECLINICAL CURRICULUM ON RATIONAL LINES

The Editor, *Journal of the I. M. A.*, Calcutta.

Sir,—Every medical college in India has its own courses and syllabuses. The universities have wisely or unwisely left the matter to respective boards of studies. The Indian Medical Council has sent round an Inspection Commission to report on the preclinical courses and instruction. This report indicates how varying are the courses and methods as well as the distribution and time of study of the preclinical subjects, and the arrangements for teaching. Though the Indian Medical Council made certain recommendations, these have not yet been considered or carried out by most colleges. It is the *student* and next to him, the *public* who have to depend on the doctors coming out of the colleges, who feel the need for a uniformity in the courses and training and examinations of the preclinical years. I trust that the following observations will provoke correspondence and lead to useful conclusions and results.

Medical studies, either of the University standard or of the diploma type, must be conducted on more practical lines. There is a tendency to teach too much of theory, too much of details, too much of each subject or specialities. These tendencies are also reflected in the examinations. The aim and scope and methods of teaching ought to be more liberal and human. Basic facts, fundamental principles, and essential data only need be taught. But these should be taught thoroughly and well—so well taught that the average pupils do not forget them ever afterwards. Minor issues controversial matters, minute details, can be looked up in any book, if need be, and these may be mentioned or the sources mentioned instead of asking the students to mug up these, to the detriment of the essential and broad principles which have to be understood and remembered. Those who have followed the recent correspondenc in foreign journal on the teaching of anatomy and physiology will recollect that the doctors are not going to be anatomists (dissecting bodies everyday of their life like the teachers of anatomy) or even histologists or experimental physiologists or biochemists. The training or preparation is that necssary to understand doctoring —health and causation of disease and cure or control of disease. For this purpose, a clear idea of the structure of the body based on the dissections of the human body (not necessarily all by himself was the only thing insisted formerly). Now, two new ideas have entered the field. One must have an equally good knowledge of the living body. One can study this on the living subject. The second and more revolutionary change is the introduction of the x-ray technique to study and teach anatomy of the human body. Now, if the students are to learn anatomy, to be doctors they must study the subject, in all the three ways, one way supplementing the other. That presupposes the old method of dissecting the whole body in the course of two years and studying regional anatomy has to be modified to give place and time, for the two other more modern methods of study. Similarly, in physiology, the time wasted on the teasing of tissues, the waste of costly and unobtainable materials to stain tissues, may be avoided by a well planned course of histology with demonstrations models and epidiascopic projections. Amphibian experiments devised to give the medical students some idea of the fundamental principles and classical experiments only need be done. The time of the student can be better utilised in learning experiments in human physiology. All the amphibian and mammalian experiments may be shown as demonstrations illustrating the lectures or better still, these courses, in amphibian and mammalian physiology may be shown as films in the course of the lectures. The physiology department should have museums for histology and for experimental physiology and human physiology and any student walking round, would have the whole course revised once. The saving of time and energy of the student and the teacher is considerable at least, enough, to meet the demand and needs of newer methods and fields of knowledge, daily coming into the realm of physiology in the medical curriculum. Experiments in human physiology are increasing in number and deserve a prominent place as they prepare the student for the clinical work.

Instead of being satisfied with looking at the heartbeat in the frog, or dog, or recording them, the student can and ought to see the human heart in action in the living subject and on the screen and record its rate and rhythm by the electrocardiogram. The study of the bronchi with lipiodal, the study of the movements of respiration, the study of the intrapleural pressure, etc., are now necessary. The movments and mechanics of the alimentary tract have to be seen with x'ray after the barium meal. The visualisation of the kidney, of the gall-bladder or the study of encephalograms cannot be omitted from the physiology classes. The handling of physiological instruments, the acquisition of the technique of use of the stethoscope the sphygmomanometer, the ophthalmoscope, perimeter, etc., require time and practice. Eliciting of sensations, reflexes, etc., require training. All these have to come in and the old methods and contents of teaching should give place to the recent and more rational methods of teaching the medical student, giving what is really preclinical training. Biophysics, biochemistry, comparative and general physiology have all to be taught in due proportions, giving priority and prominence to human physiology, which was not much known till recently and which has to be studied now, as the basis of medical practice.—I am, etc.

Vizagapatam, Medical Educationist.
24-1-44.

MANUFACTURE OF UNDERSTRENGTH DRUGS

The Editor, *Journal of I. M. A.*, Calcutta.

Sir,—Recently some medical practitioners complained to me that many cases of malaria occurring this year were resistant to Quinine. I had an attack of malaria and three injections of quinine bihydrochloride supposed to contain ten grains of the drug were given to me. I was temporarily cured and fever

reappeared after 15 days. This led me to suspect that the ampoules used may be containing lesser quantity of quinine than indicated on the label.

I consequently analysed nine ampoules of quinine bihydrochloride of different Indian makes. The result of analysis is given below:

The no. of ampoules analysed	9
The no. of ampoules found genuine	4
The no. of ampoules which contained 75% less of quinine bihydrochloride, than what was indicated on its label	3
The no. of ampoules which contained 70% less of quinine bihydrochloride. than what was indicated on its label	1
The no. of ampoules which contained 20% less of quinine bihydrochloride, than what was indicated on its label	1

The ampoules were manufactured by pharmacies located in U.P., Bengal and Bombay.

There is a great scarcity of quinine in this country and some dishonest manufacturers are putting lesser quantity of quinine than what is stated on the label of the ampoule. It is very likely that the same state of affairs exist in manufacture of all other injections as well as costly and scarce drugs. One does not know when the Government of India will enforce the Drugs Act in this country and it is neither in the interest of the profession nor the public to sit quiet over the matter and pray for early enforcement of the Act. I would suggest that the Indian Medical Association should appoint a Foods and Drugs Committee, as appointed by the American Medical Association. This Committee can arrange to get the services of any private but respectable laboratory in the country and get analysed all the important drugs and chemicals on payment of fees and can issue certificates of approval of drugs and pharmaceutical preparations manufactured by various Indian concerns on payment of fees. If the Indian Pharmaceutical Manufacturers co-operate with the Indian Medical Association, then the scheme will not be a losing concern and will meet its maintenance expenses. Of late, many mushroom pharmacies have cropped up and one does not know what kind of stuffs they are dumping in the market and sooner the problem is tackled, the better.—I am, etc.

Surat,
25-3-44.

A. H. PALIT,
Public Analyst,
Surat Borough Municipality.

SPURIOUS QUININE AND EMETINE AMPOULES

Sir,—You are perhaps aware that the present high prices and non-availability of chemicals have led unscrupulous persons to flood the market in Bombay, Calcutta and elsewhere with spurious medicinal ampoules of quinine and emetine alleged to be made by us and similar recognised firms. You can well appreciate the extent of the mischief that this fact means to both the patient and the doctor when we say that according to reliable reports received by us these ampoules are being offered for sale, loose or packed, at a price much below the present cost of the raw materials required for their manufacture.

Considering, therefore, the seriousness of the matter may we, as one of regular advertisers, count upon you to help arresting the spread and use of these spurious medicines by putting doctors and consumers on their guard by means of suitable warnings published in the 'Notes and News' columns of your magazine?

It may be added in this connection that we are doing our bit in the matter by publishing our own warnings in the advertisement columns of lay papers.

Expecting your co-operation.—I am, etc.

Calcutta,
11-3-44.

A. GHOSH,
Publicity Officer, B.C.P.W.

AN APPEAL FOR RS. 5,00,000 FOR THE "COLLEGE OF PHARMACY FUND"

DEAR MADAM/SIR,

In the name of our common humanity, to relieve preventible human suffering of millions of our fellow-beings from avoidable disease and premature death, due to the Man-made Drugs Famine in India, I appeal to your large-hearted generosity to contribute your donation to help my Association in raising Rs. 5,00,000. for our **"College of Pharmacy Fund"**, before June, 1944. My Association has resolved, so far as possible, to establish a College of Pharmacy in Bombay, **in collaboration with our Bombay University,** by next June, with the main object of training and after qualifying examinations, turning out a number of Pharmacists, every year. They will be competent to manufacture cheap and pure Medicines of standard strength and quality, in local Pharmaceutical factories, and **thus help in liquidating the Man-made Drugs Famine in India.**

In case, you are connected with a Charity Trust, or any Institution, which is empowered to help a benevolent scheme like this, may I appeal to you to kindly exert your influence to secure a big donation for such a humanitarian cause, for which we shall feel much thankful to you. In addition to any Donations, Gifts or Endowments for the College to perpetuate the memory of persons of your choice will be thankfully received.

Please help our medical profession in our mission of mercy, to save our suffering brothers and sisters from the torture of preventible disease and death due to the Man-made Drugs Famine, and so enlarge the field of human happiness, by sending your contribution promptly to our Fund in the name of our common humanity. Yours etc.,

Jenkin's House, Mereweather Road,
Apollo Bunder, Bombay,
24th January, 1944

K. K. DADACHANJI,
President, Bombay Medical Association (I.M.A., Bombay Branch),
and Chairman, College of Pharmacy Fund.

REVIEWS

A SCHEME FOR A COLLEGE OF PHARMACY FOR BOMBAY—By Dr. K. K. Dadachanji, President, The Bombay Medical Association.

Pharmaceutical science is one of the most neglected of the scientific disciplines and very little attempt has so far been made by the Provincial Governments or the Universities in India (with the exception of the Benares and Andhra Universities) to institute courses in this important subject and to impart proper training in this field, which has a direct bearing with the drug industry of the country. The effort made by the President of the Bombay Medical Association to establish a College of Pharmacy in Bombay, therefore, is commendable and his appeal is well worth the support of all progressive and generous citizens of the Province of Bombay and elsewhere.

The first awakening of consciousness regarding pharmaceutical training in India was brought about by the Report of the Chopra (Drug Enquiry) Committee as far back as 1930-31. At that time a strong plea for immediate institution of measures for imparting a proper and adequate training in pharmacy on the lines existing in America and Great Britain was made so that the drug industry in India may grow, and indirectly, scientific medical practice may permeate throughout India in place of quackery and charlatanism by the supply of drugs and medicines of proper quality and potency. The 'Report' of this committee met with the same fate as many other 'Reports' and was relegated to the archives in the Government museum; and today, after another 15 eventful years, India is still complacently looking at the old scene and is again agitating and cogitating on the need for a College of Pharmacy in Bombay. A most distressing situation indeed!

This reminds the writer of the committee appointed by the Government of Bengal in 1938-39 to consider the feasibility of establishing a 'College of Pharmacy' in Bengal (with the offer of a grant of Rupees two lacs from Dr. Anklesaria of Bombay). The Report of this committee (Report of the College of Pharmacy Committee, Government of Bengal, Published by Bengal Government Press, Alipore, Calcutta), voiced more or less the same feelings as Dr. Dadachanji, has done in his scheme. In fact, one is tempted to think that Dr. Dadachanji has taken his inspiration in working out of the details of the scheme from the above 'Report'. Let us hope that the advice and guidance in this matter, which went unheeded in Bengal, will be responded to in Bombay and a 'College of Pharmacy' would soon come into being.

Dr. Dadachanji's scheme for a 'College of Pharmacy' is essentially sound. The only remark that the writer would like to offer is with regard to the standard of training prescribed for the 'Diploma in Pharmacy' course. In Bengal it was considered that the minimum basic qualification should not be beyond the Matriculation standard of Indian Universities. A two-year curriculum was recommended with generous attention towards practical work and 'apprenticeship'. In Dr. Dadachanji's scheme the entrants to the Diploma course are expected to be Intermediate in Science' and a 2-year training period after this is enjoined without much stress towards apprenticeship training. While such a programme may be considered ideal from certain aspects, there will be practical difficulties in that the country is not yet ready to give such a diploma-holder adequate status and financial return. Most of these scholars, it is presumed, will be absorbed in the dispensaries, drug stores and hospital pharmacies, which are not in a position to pay decently for qualified people when they can get 'quacks' for only a small pittance. It is perhaps necessary in the first instance to push through the 'Bombay Pharmacy Act' by which qualified pharmacists would be protected before the standard aimed at by Dr. Dadachanji can be attained.

Dr. Dadachanji deserves credit for the forceful way in which he has presented his essential practical points. It is to be hoped that he will not leave the matter at the 'Scheme' stage but will see that the college is established. He should also try for an 'All-India Pharmacy Act' instead of simply a Provincial legislation and should make every effort that the 'Drugs Act, 1940' is also enforced by Government of India. Once these two legislative measures are enacted, schemes for Colleges of Pharmacy in every province will automatically bear fruit. Public opinion must also be mobilised to give the pharmacists the status as 'scientific workers' due to them. 'Pharmacy' is a handmaiden to 'Medicine' and both must move side by side if any lasting benefit is aimed at in medical relief, public health improvement, industrial regeneration. and national well being.

B. N. GHOSH

"NEED FOR CO-OPERATIVE RESEARCH IN INDIAN CHEMICAL INDUSTRY"—Presidential Address by Sir S. S. Bhatnagar, KT., O.B.E., F.R.S., etc.

In his Presidential Address at the Conference of Manufacturers of Chemical and Pharmaceutical products and representatives of Universities and Research institutions held at Bombay on the 6th November 1943, Sir Shanti Swarup Bhatnagar emphasised the need for co-operative research in Indian Chemical Industries and recommended the establishment of research associations in India after the model of the research associations functioning in the United Kingdom.

Both in industry as well as in academic fields, all progessive scientists are now of one opinion regarding co-operative research and Sir Shanti Swarup has only voiced forcefully the feelings of many thinkers. The examples he has given of the achievements in Great Britain through co-operative research by the various research associations operating under the auspices of the Department of Scientific and Industrial Research, are worth noting with pleasure and admiration. One naturally turns around to assess the achievements of a similar body in India, the Board of Scientific and Industrial Research of which Sir Shanti Swarup is the Director. Indeed, he has given a short account of the progress in this direction made in India since the creation, during the present war, of the Board of Scientific and Industrial Research. India now manufactures such heavy chemicals as Sulphuric Acid, Caustic Soda, Soda Ash, Chlorine, Chlorosulphonic Acid, Formaldehyde in quantities much higher than the pre-war period. She is also well ahead in the field of coal tar distillation products. but when the production figures in India are compared with available figures of production of these items from such countries as Great Britain, America and

Germany, the progress achieved by Indian industries does not seem to be adequate. Much still remains to be done and should be done with a resolute will and on a co-operative basis unknown in India before.

Sir Shanti Swarup has rightly pointed out that to make any headway in industrial research and to derive real benefit from research associations financial aid on a much higher scale than at present is required. Both State help and help from industrialists and industrial organisations are called for.

It is not necessary, Sir Shanti Swarup has rightly pointed out, to start new buildings and new laboratories for every research association formed. This will result in freezng of assets in a way which cannot be always considered desirable. Existing laboratories, either in Government institutions, commercial concerns or universities may be utilised for the purpose and equipped properly for the prosecution of a suitable research project. A grant could be made for such research by one organization or jointly by a number of organizations actuated by the same motive. Thus a group of pharmaceutical organizations could very well join together and give a grant for drug research in any pharmacological or pharmaceutical laboratory. With better times and finances forthcoming after the war, organized and well-equipped laboratories could be set up where ambitious research projects could be undertaken on modern up-to-date lines.

Sir Shanti Swarup deserves our gratitude for clearly placing before the commercial bodies and industrialists the value of co-operation and research. We hope his address will be widely read and acted upon by those interested in scientific and industrial development in India.

B. N. GHOSH

MEDICAL JURISPRUDENCE AND TOXICOLOGY—By John Glaister. 1942. Seventh Edition. Pages vii+671. Demy 8 vo. With 132 illustrations, several in colour. Published by E. & S. Livingstone, 116 & 117 Teviot Place, Edinburgh. Price 28s. net, postage 9d.

The seventh edition of this well-known standard work appearing within these difficult times is itself a proof of its popularity and of the need it meets. This edition has been completely recast and almost entirely re-written, so that it is smaller than its predecessor, small typed portions being eliminated and much superfluous and discussive details deleted. Many illustrative cases cited are fresh, the most interesting and fascinating one being that of Ruxton Double Murder with mutilations and purposive removal of parts of the bodies. This case has been dealt more fully with anatomical, radiographic and photographic illustrations showing a novel comparison of skulls and portraits of the victims superimposed upon each other which helped to place identification beyond doubt. The section on identification of hair is a distinctive feature of the book, and that on examination of blood stains and blood grouping is at once clear and concise. The chapter on toxicology has been very much abridged and the poisons described in such a manner that it will be very useful specially for the students to undertsand and remember this difficult subject. This work has maintained to the full the high standards which have put it in the front line of the smaller text books on medical jurisprudence. It is eminently a book for the senior medical students preparing for their final examinations, and for the general physicians and medicologists as well, all of whom will profit from a perusal of its easily read pages.

S. K. BOSE

THE MEDICAL COLLEGE MAGAZINE, CALCUTTA—Vol. XI, No. 1, October, 1943.

We congratulate the Editor for bringing out a journal of 112 pages at this difficult time. Most of the articles are written by the teachers and only a few are from the pens of the students. Of the 24 articles only four articles had anything original in them. Others are just chapters from any text book. Does it reflect, we wonder, that no attempt of research is being done in this premier institution of Bengal? We appealed to the authorities of this journal last year to embody the reports of departmental work but it seems that though many of the teachers contribute original articles in outside journal, they do not care much for their own journal. Furthermore, may we suggest that the teachers would direct the students and house physicians to contribute more original observations and case notes?

ILLUSTRATIONS OF SURGICAL TREATMENT—Instruments and Appliances (Second Edition)—By Eric. L. Farquharson, M.D., F.R.C.S.E., MAJOR R.A.M.C. Published by E. & S. Livingstone, 116 & 117 Teviot Place, Edinburgh.

In this book the author seeks to describe by illustrations rather than by giving bulky and long descriptive details, the various methods of treatment which it is difficult or impossible to visualise without illustrations. The book has been divided into two main portions. The first portion deals with various infusions and transfusions and the treatment of fractures and of the commoner orthopædic conditions. The last portion consists of illustrations of instruments and appliances in use in general surgery. This latter will be of great help in assisting students and post-graduates to prepare for examinations. The descriptions of the treatment of fractures and of the various methods of applying extensions are brief but amply clarified by excellent photographs and illustrations in which the book abounds. Clear but short details of after-treatment are also included for the different varieties of treatment described. The need of such a book as a reference not only for house officers but also medical practitioners is great. We recommend this book to the practitioners in India to whom probably a book like this would be most useful as a guide in view of the paucity of the facilities for post-graduate training or refresher courses in India.

KARUN S. RAY.

THE MEDICAL ANNUAL—A Year Book of Treatment and Practitioner's Index. Sixty-First year, 1943. Edited by Sir H. L. Tidy and Dr. A. Rendle Short. Published by John Wright & Sons, Ltd., Bristol. Price 20s. net.

Further work is reported on the antibacterial products of fungi, Flemming's penicillin is still in the lime light of world medical literature. It has been found that gram-positive organisms are easily inhibited by penicillin while gram-negative bacteria with a few exceptions *e.g.*, the gonococcus and meningo-

coccus are resistant. In an extremely pure form it inhibits the growth of staphylo. aureus at a dilution of 1 in 25,000,000 completely and at 1 in 160,000,000 partially. The Oxford school has so far been unsuccessful in obtaining penicillin in a crystalline form while Hobby and her colleagues in U.S.A. claim to have obtained crystalline salt of penicillin. Clinically, penicillin is most useful in the treatment of sulphonamide-fast strains of streptococci, pneumococci and gonococci. The other product gramicidin obtained from the autolysed culture of B. Brevis has been found to possess great power of lysing gram-positive though not gram-negative bacteria. Experimental results on animals against gram-positive bacteria are highly promising. Among a dozen of other fungal products these two have a real future. As both of them are rather difficult to obtain in large quantity for commercial purposes, perhaps ordinary people will have to wait till they are synthetically produced.

Five more new members have been added to the family of Sulphonamides during the year under review: Sulphadiazine, Sulphamethazine, Sulphapyrazine, Sulphaguanidine, Succinylsulphathiazole. From the clinical reports it seems that the first three have actions and toxicity similar to other sulphonamides. The search for a nontoxic sulphonamide has not yet been fruitful. Sulphaguanidine. a newer find, has been found successful in the treatment of bacillary dysentery and dysentery carriers. In typhoid fever it is useless. Of the last two, administration of succinylsulphathiazole is more effective in minimising the effects of accidental soiling of the peritoneal cavity in operations on the large gut. We have yet to find a sulphonamide for ulcerative colitis.

The results on the use of sulphaguanidine in cholera are conflicting. Further trial should be given to this drug before any conclusion is drawn. Promin, a sulphonamide, eradicates Pl. knowlesi infection in rhesus monkey but the effect of promin, sulphadiazine, and sulphathiazole on human malaria has not been encouraging. Malaria now being a distressing Indian health problem due to lack of quinine and any antimalarial measure on a wide scale, the report of a new antimalarial alkaloid, sinine, prepared from the root, bark and leaves of a Chinese species of ash, Fraxinus malacophylla, is interesting. The tree is abundant in China and grows readily. The clinical results are encouraging but yet unconfirmed by others. Investigations to identify the tree and the anti-malarial properties of Sinin are desirable in this country where malaria alone has claimed millions of casualties in 1943.

With the shortage of emetine in Indian market and meagre production of iodochlorohydroxyquinoline compounds, the treatment of amœbiasis has become difficult. Favourable clinical reports from China on the use of seed kernels of Br. antidysenterica in amœbiasis should be noted. This plant grows abundantly in Abysssinia and controlled trial of the drug should be given in this country immediately.

Miniature mass radiography of the chest is now being employed to detect tuberculosis in individuals before clinical symptoms have developed. Results of investigation in the Royal Navy, Royal Air Force and civilians are given. The difficulty experienced in submitting people to such examination and the question of financial help to diseased persons are now

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OBITUARY

RAI BAHADUR HARENDRA NATH DAS, M.A., M.D.

Death occurred of Rai Bahadur Dr. Harendra Nath Das, M.A., M.D., a leading physician of Calcutta, on the 13th March, 1944. Dr. Das was intimately connected with the medical institutions of the province being Honorary Life Member of the Medical Education Society of Bengal. He was a professor of the Carmichael Medical College and physician of the College Hospitals, the Sambhunath Pandit Hospital, Professor and Examiner of the Post-graduate Department of the Calcutta University, Visitor of the Campbell Medical School and a member of the Executive Committee of the Leper Asylum under the Church Missionary Society of Calcutta. He compiled a few medical books which received appreciation from the scientific world. Dr. Das was awarded the title of Rai Bahadur in 1924 in recognition of his services to the country.

The Rai Bahadur was a social worker. He was the Commissioner and Councillor of the Calcutta Corporation from 1923-30, Governor of the Refuge, Calcutta, Hony. Medical Advisor of the Co-operative Training Institute under the Government of Bengal and to the Olympic Games, Calcutta.

Throughout his life Dr. Das took a keen interest in the educational, social and physical uplift of the poor and destitute.

The Rai Bahadur leaves behind his wife, five sons, four daughters and a host of friends to mourn his loss.

May his soul rest in peace!

(*Continued from previous column*)

being solved. Propaganda regarding the optimistic outlook of cases detected early, education of the people about tuberculosis, and assurance of employment of those who respond well to treatment have helped much in this campaign.

Instructive chapters have been incorporated on burns of war and the plastic surgery of burns of the hand. Report of successful treatment in 8 cases of acute hæmatogenous staphylococcal osteomyelitis by sulphathiazole is given. But it still lacks confirmation in other hands since it is believed that sulphathiazole is not bactericidal to all strains of staphylococci. Two medical students in London and one in Bristol have observed that during the heavy air raids on the two towns, the number of perforated gastric and duodenal ulcer cases showed a remarkable increase. They suggest that anxiety, with perhaps too much smoking and alterations in food habit are the cause.

For want of space it is not possible to discuss the other features of the Medical Annual. Though diminished in volume it has not lost any of its former brilliance in cautious and detailed summary of notable contributions during the year. A dislocation in the exchange of medical literature between different countries still exists mainly due to difficulties of transport and shortage of paper. The Medical Annual brings to the practitioner everything in a nutshell. He will still find it a mine of information.

B. P. NEOGY.